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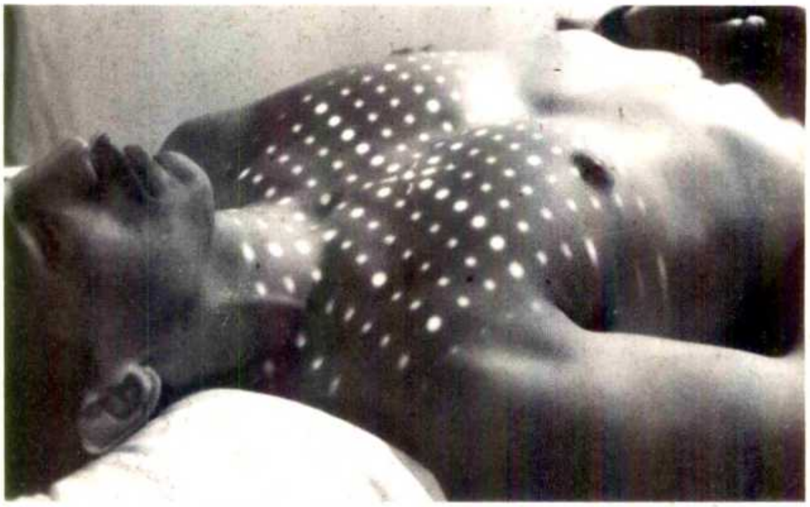

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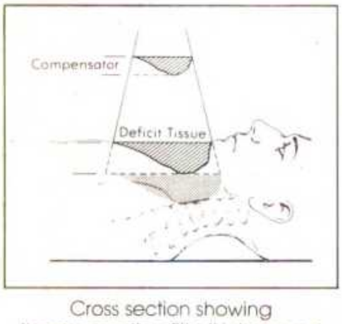

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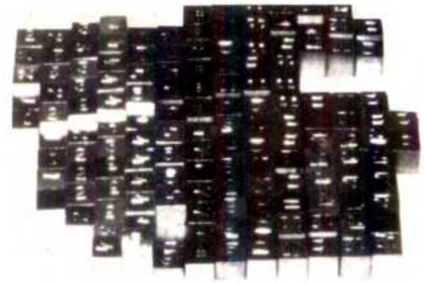

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Magnetic resonance: boundless possibilities . . . or possible boundaries*

By I. R. Young, FRS

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(*Received March 1989*)

Dedication

Silvanus Thompson was a cultivated and learned man in the sense recognized by the Victorians, but, sadly, largely a thing of the past. He touched many things, improving them all, including translating Gilbert's *De Magnete*. When he was active, the use of electricity and magnetism in medicine were matters of keen interest, but one can only guess at what a world adapting to Röntgen's wonderful discovery would make of today's evolution of a magnet-based method of observation and measurement into, possibly, the most powerful *in vivo* diagnostic tool yet discovered. However, it is a reasonable guess that a mind as flexible and receptive as that of Silvanus Thompson would have embraced it with euphoric excitement.

Introduction

Perhaps the single most exciting thing about whole-body magnetic resonance (MR) is its scope. It is possible to design procedures for an almost indefinite repertoire of different studies, each more elaborate than the last and capable of more refined interpretation. The only snag—often mentioned with a sense of resignation—is that the process may take a long time. This reflects the fact that the sensitivity of the technique is limited, and that signal-to-noise ratio (SNR) considerations affect everything that is attempted.

Nuclear magnetic resonance (NMR) aficionados are inclined to cloak their activities with a miasma of acronyms and jargon, leading to *in vivo* spectroscopy, in particular, being viewed as almost impenetrable in its mystique, though imaging can often seem little less opaque. In this paper we propose that the destruction of this false perception gives rise to some of the greatest hopes for the future of the modality.

On the one hand, the paper reviews briefly the restrictions on performance that are likely to limit the results of *in vivo* NMR in the future, while, on the other hand, it attempts to show how interdependent the various techniques are, and that familiarity with one method allows constructive and intelligent application of others. Moreover, it is not difficult to locate the signposts that suggest what MR might do well, and, even more important, what it is never likely to handle with the same effectiveness as other approaches.

Limitations

The basic problem of NMR (its lack of sensitivity) has already been mentioned; more often than not, however, actual performance is limited not by excessive noise but by signal-dependent artefact (with the most commonly recognized problems being associated with abdominal wall motion). However, any irregularity or instability during the data acquisition process using the almost universally applied spin-warp method (Hutchison et al, 1980) results in the generation of spurious signals in the phase-encoding direction (*i.e.* in the direction(s) of the spatial encoding applied after excitation but before data acquisition). The resultant data usually look noisier, though that is not because there is more noise, but because some of the signal has been quasi-randomly redistributed across the image and its peak intensity has been lost.

At first sight the consequences are the same because additional averaging (taking more time per study) may improve matters to some degree (*cf.* Stark et al's work in the liver, 1987), but, ultimately, the encouraging thing is that whereas the true system noise can only be reduced within fairly narrow limits, the artefact can be reduced to a very low level as techniques improve. Even in a low-field machine, such as the 0·15 T unit at Hammersmith (Young et al, 1982a), artefact is typically between four and eight times the true noise level in patient studies. The solution to the problem will not be easy as, assuming all machine instabilities and non-linearities are eliminated completely, patient movement has many different aspects and effects, some of which are a function of the strength of the main magnetic field while others are independent of it. Respiratory motion, for example, causes problems in at least four different ways, two of which are field dependent.

1. Direct effects resulting from displacement of a signal

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*The 1989 Silvanus Thompson Memorial Lecture, delivered at the British Institute of Radiology in London on 21 February, 1989.

source from one point in the image matrix to another.

2. Changes in the radiofrequency (r.f.) field strengths resulting from the expansion and contraction of the body varying the electrical load placed on the r.f. coils.
3. Variations because the r.f. fields are not perfectly homogeneous so that, as a piece of tissue with voxel-size dimensions moves from place to place, it may be excited to different degrees, and the signals from it detected with differing sensitivities.
4. Alterations in the apparent spin–spin relaxation time constants as a voxel-sized unit of tissue moves in an inhomogeneous main field.

Factors 2 and 4 are field dependent.

There are probably other effects; the point to note is that there is no one correction that can control all four at once. If other potential sources of motion (heart motion, pulsatile blood flow and cerebrospinal fluid (CSF) flow, peristaltic motion and involuntary movement such as swallowing or eye motion are included, it is apparent how much scope there is for work in this

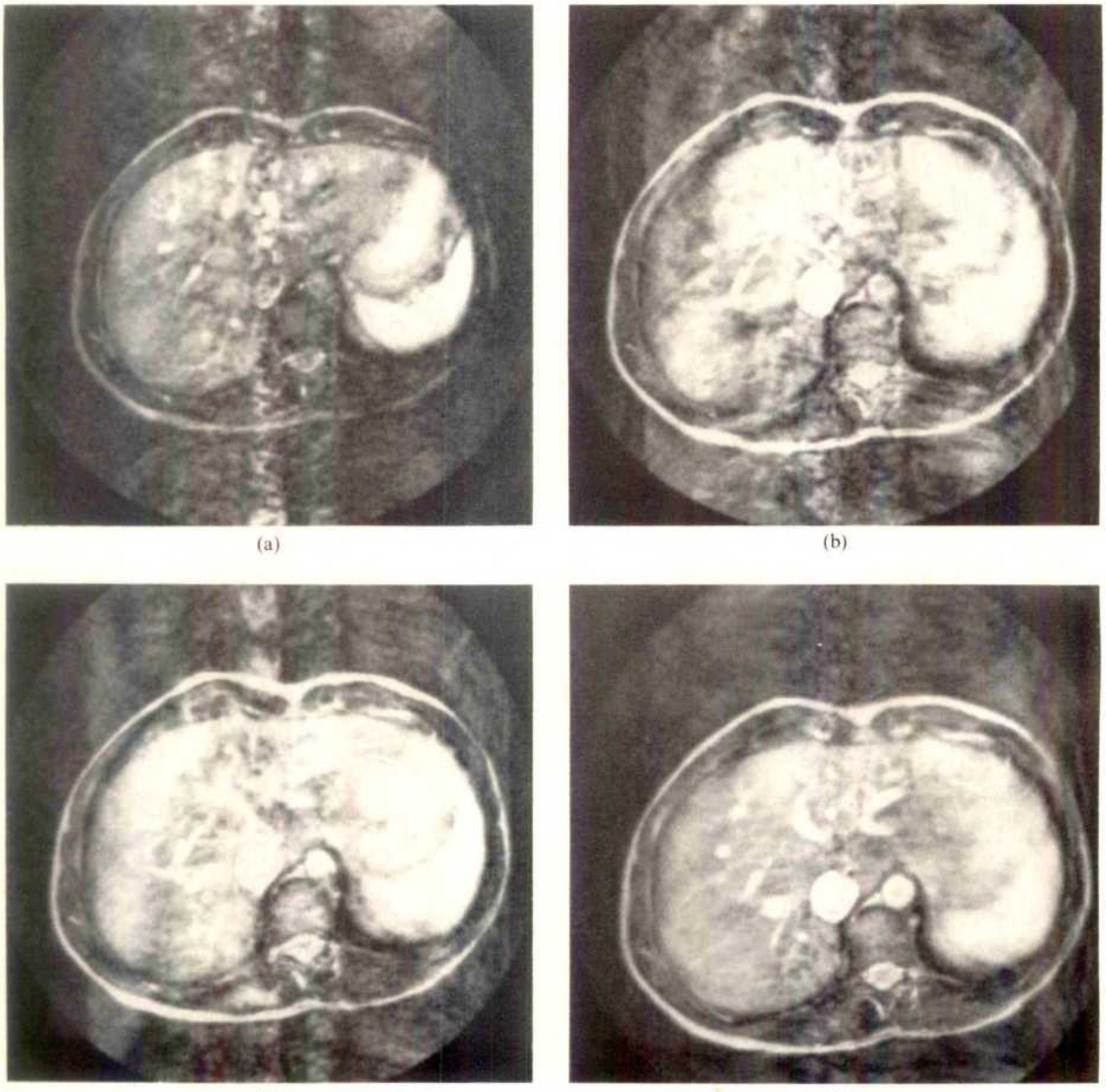
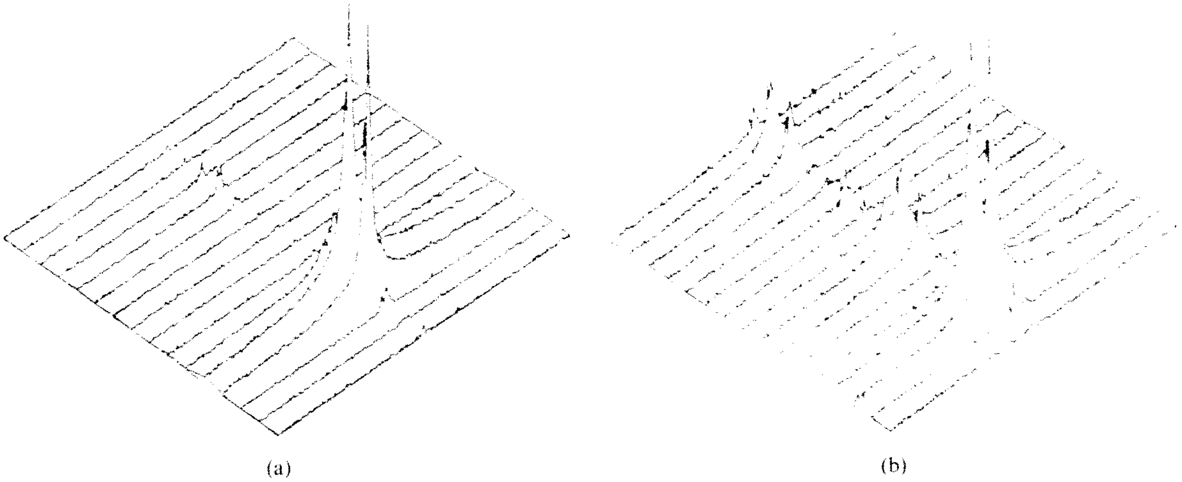

(a) (b) (c) (d)

Figure 1. Four images showing the impact of additional motion artefact control mechanisms on abdominal images. The data are from a volunteer, acquired with an image matrix of 256 × 256 (employing two data inputs for each view) and slice thickness of 6 mm. (a) No motion artefact control, (b) MAST only, (c) MAST and ROPE and (d) MAST, ROPE and ECG gating.



(a) (b)

Figure 2. Effects of motion on spectroscopy. The stackplots were the result of one-dimensional phase encoding, 16 slices being shown, from 256 acquisitions. (a) Phantom at rest, and (b) phantom moving with a period of around five times the repetition rate of the experiment.

area. Ironically, controlling one or two parameters may just make it obvious how much more has to be done (Young, 1987). Thus, in an abdominal study, the use of a method called MAST (motion artefact suppression technique) (Pattany et al, 1987), which is a sophisticated system for gradient nulling, may even degrade images compared with doing nothing unless it is accompanied by respiratory ordered phase encoding (ROPE) (Bailes et al, 1985) to control artefacts in the phase-encoding direction.

Figure 1 illustrates the problem. The four images show an image without any form of artefact correction, one with MAST, one with MAST and ROPE and both of these techniques with cardiac gating. Even with all these techniques, artefact is still present, and other (and better) methods are needed, as three of the four problems in the previous list are not controlled by these techniques. This is well illustrated in that application of both ROPE and MAST makes it clear how much artefact is arising from variations in signal due to the pulsatile flow of blood through the major vessels, emphasizing the need for electrocardiographic gating, and so it continues. However, the use of more techniques involves more setting up and, usually, more time. Rapid imaging methods such as echo planar imaging (EPI), as pioneered at Nottingham (Mansfield, 1984), offer a path round most of the motion problems, but at the expense of a decreased SNR.

It is likely that much *in vivo* spectroscopy is as badly affected by artefact as imaging though this is much harder to recognize in spectra. Artefact produces a reduction in SNR, but the symptoms are less revealing as to the source. The various techniques used in the formation of regions from *in vivo* spectroscopy are very different in their response to any given error, so that it is much harder to generalize about artefacts than it is with imaging. On the other hand, because sensitivity is so low with spectroscopic studies, it is even more important to control artefact. The general strategy of selecting regions that are large enough to give a good SNR means that voxel sizes of 30 mm × 30 mm × 30 mm and more are often used, particularly in phosphorus spectroscopy. It is interesting to speculate as to how much of the current struggle to generate clinically useful spectroscopic data stems from a genuine lack of signal variability and how much comes from partial volume effects that are gross compared with those found with any other imaging modality.

It is easy to demonstrate the effect of motion artefact in spectroscopic studies, as shown in Fig. 2, but much harder to assess them in a particular clinical study. The results in Fig. 2 were obtained from a small phantom (a bulb) filled with water. One-dimensional phase encoding (Bailes et al, 1987) was used in both experiments with a slice thickness of 4 mm, and 16 slices were acquired as shown in the stackplot in Fig. 2a with the phantom at rest. In Fig. 2b, the phantom was oscillated in the direction of phase encoding with an amplitude of 10 mm and a period about five times that of the pulse repetition time. The dominant appearances in Fig. 2b are a redistribution of signal and apparent increase in the noise (which is actually an artefact of the way the results are normally displayed). The problems of artefact in spectroscopy are exacerbated relative to non-standard imaging procedures [such as the mapping of phase differences in measuring flow (Bryant et al, 1984)] because the lack of sensitivity means that it takes a long time to perform each check on system behaviour, and several of these are necessary to assess fully what is happening.

Spectroscopic studies may be more badly affected by an MR limitation other than imaging. The spin–lattice time constants (T_1) are very long for many metabolites, and long recovery times penalize all MR procedures, particularly where they are much longer than the spin–spin relaxation time constants (T_2). As long as T_2 is not too short, the ratio T_2/T_1 is a useful figure of merit, and optimum SNR would be obtained from circumstances where it is both close to unity and uniform from one tissue to another. On this basis, it is possible to predict that results of proton imaging of the central nervous system could be better than for many other regions of the body; similarly, it is possible to forecast that phosphorus spectroscopy of the liver could be easier than that of the brain.

Quantification is probably more important in spectroscopy than imaging and this is affected more by uncertainties about time constants than anything else. Even measuring the ratios of peaks in a single spectrum makes implicit assumptions about their relative time constants and absolute quantification, necessary to reveal an overall loss of all the metabolites of a nucleus (Bates et al, 1988), may not be practicable.

However, because metabolite relaxation times are often much longer than those of hydrogen in proton imaging, the time taken to evaluate them can become quite extended. Methods of rapid operation, in a manner analogous to imaging, are not so applicable to spectroscopy since a long time must always be allowed for data acquisition in order to resolve the spectral components and the minimum useful value of the repetition time (TR) (ACR, 1983) is of the order of 250 ms compared with 20–25 ms in imaging.

Opportunities

In spite of these restrictions, the future seems to offer the prospect of an ever-expanding range of applications for *in vivo* magnetic resonance. The range of applications in diagnostic imaging is apparent from the literature, and there is no need to enumerate it here. Rather, I will concentrate on applications and possibilities that extend far beyond conventional radiology into physiological and biochemical studies, in order to show that they are properly part of what is, essentially, an imaging concept.

The opportunities will be discussed under four categories: (1) flow measurement at all levels, (2) mapping of the evolution of haemorrhagic deposits, (3) spectroscopic studies and (4) monitoring of therapy. The last is a little different from the first three in that it is, in essence, an example of their collective application, but it offers the possibility of extending the application of radiological methods to therapy well beyond the limit of interventional procedures as at present practised, though there is room for only the most cursory reference to it in this paper.

Flow observation and measurement

The endeavour to use NMR for monitoring *in vivo* flow precedes its clinical application in imaging and whole-body spectroscopy. In principle, the techniques used today were developed by Singer and his colleagues (1959) and Packer (1969). Researchers noticed early on (Young et al, 1982b; Bradley, 1984) that the appearance of flowing material in images was very variable, suggesting that mapping flow justified serious exploration. Since then, flow work has taken two main paths: first the development of analogues to conventional angiography, which is, so far, non-quantitative, and secondly the exploration of methods of measuring flow velocity. Studies have ranged from observation of very rapid flow patterns in major vessels to tissue perfusion, while blood acceleration and turbulence has also been successfully demonstrated.

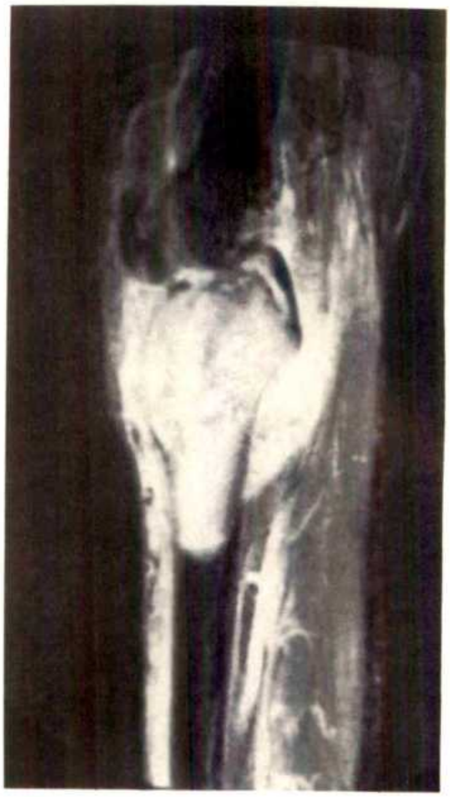


Figure 3. Short tau inversion–recovery image of the leg of a patient with a tumour showing the pseudo-angiographic appearance of the residual signals (though the image is dominated by the lesion itself).

Angiography

Although a variety of methods have been proposed (Nishimura et al, 1987; Dumoulin et al, 1988), most use the same principle. Two sets of data are acquired, in one of which the signals from moving spins are modified relative to those at rest. The two data sets are then subtracted to leave a pattern containing signals only from regions where there has been flow. Other methods are variants of the inversion–recovery technique based on the short time to inversion–recovery concept (Bydder & Young, 1985) to cancel as much as possible of the signals from tissue with a relatively short T_1 (such as fat and muscle) leaving the signal from blood, which has a relatively long T_1. This method has the attraction of needing only a single data acquisition, but suffers from the problem that the T_1 values of many lesions are at least as great as that of blood, remaining apparent in the image, as shown in Fig. 3.

A problem with MR angiography is its spatial resolution: typically, vessel diameters need to be in the 0.5–1 mm range before being visible. A second difficulty is that, since sensitivity is low, long periods of data acquisition are needed from basically motionless anatomical structures. As a consequence, satisfactory results have been obtained using full three-dimensional data acquisition allowing volumetric reconstruction of the vessel pattern in the neck and head, though no-one has yet produced a credible coronary angiogram. However, progress is being made through the use of volume data acquisition and sophisticated but cheap work stations, and clinical applications are now appearing.

Measurement of rapid flows

Methods of flow measurement using the magnitudes of signals, in spite of a variety of attempts (Crooks & Kaufman, 1984; Mueller et al, 1985), have proved to be unproductive. There are a variety of reasons for this, though many revolve round a lack of knowledge of the precise form of the volume of material that has been excited (Young et al, 1985). Experiments based on the observation of phase changes (Moran, 1982; Bryant et al, 1984) have proved to be much more productive. In principle, these methods depend on acquiring two data sets, in one of which an additional pair of gradient pulses are included (or an existing pair are altered in magnitude, duration or separation). A typical arrangement using a spin–echo sequence is shown in Fig. 4, and the relevant parameters are marked. If the velocity of flow is v, the amplitude of the gradient pulses (which are the same in the spin–echo experiment shown) is G, their duration is t_D and the interval between their leading edges is t_p, then the phase difference (ϕ) obtained between the phases observed from the two sets of image data is given by:

$$\phi = \gamma G t_p t_D v$$

where γ is the gyromagnetic ratio. (Note: the phases of the voxels in any one image are determined by a whole host of machine parameters, hence the need to work with phase differences between two data sets that are as nearly identical as possible in every respect except the one that is to be varied.) Thus flow velocity and phase are directly proportional to each other, related only by a fundamental constant and three parameters, two of which (t_p, t_D) can be controlled with extreme precision. The accuracy of the experiment is thus determined by G

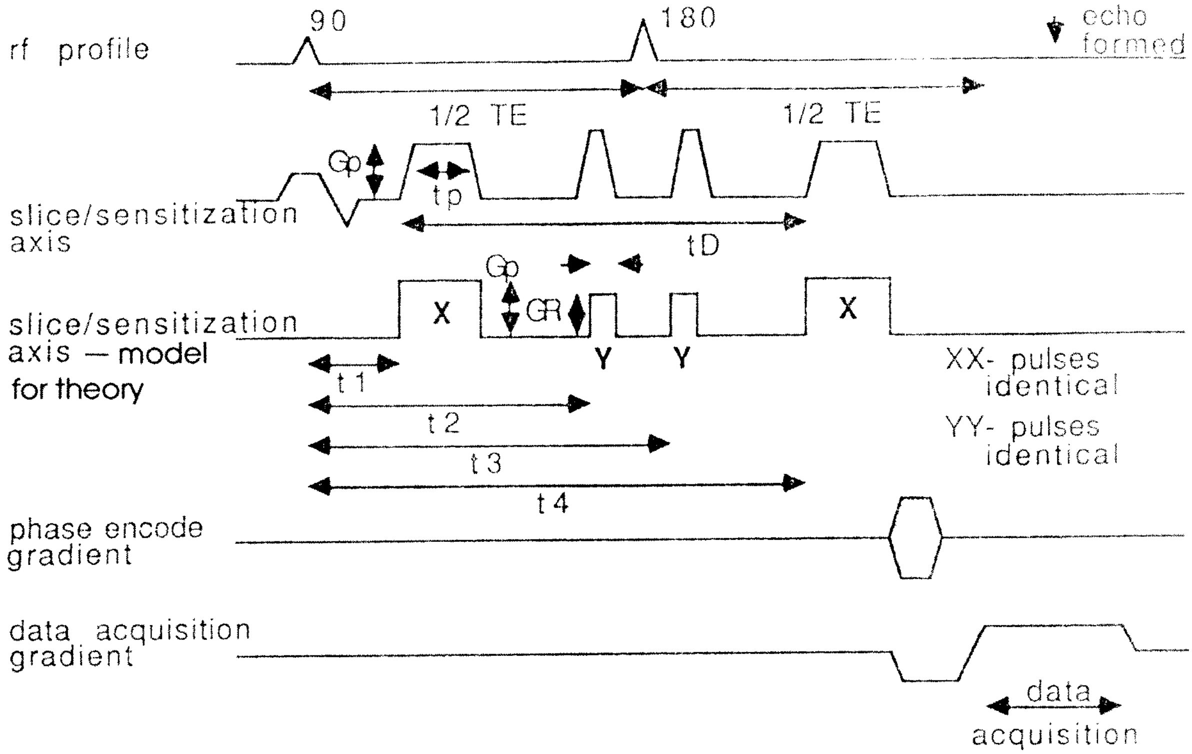


Figure 4. Diagram showing the encoding pulses added to a typical spin–echo experiment sequence, which are used to encode flow data. These extra pulses are those marked X, though variants of the method use differences between size, duration and location of the pulses marked Y. Non-moving material is rephased by the pairs of pulses, whereas moving spins are in a different field from that in which they are dephased at the time they are rephased, introducing phase differences into their signals.

(which can be 0.5% or better) and the intrinsic noise in the system.

This form of technique was first applied to relatively motion free regions such as the neck (Bryant et al, 1984) but latterly to more taxing experiments in the heart. Longmore and his colleagues (1986) have demonstrated a further variant in which acceleration has been mapped during the cardiac cycle, while regions of turbulence are apparent through loss of signal when lower-order motion effects have been corrected for. Using these

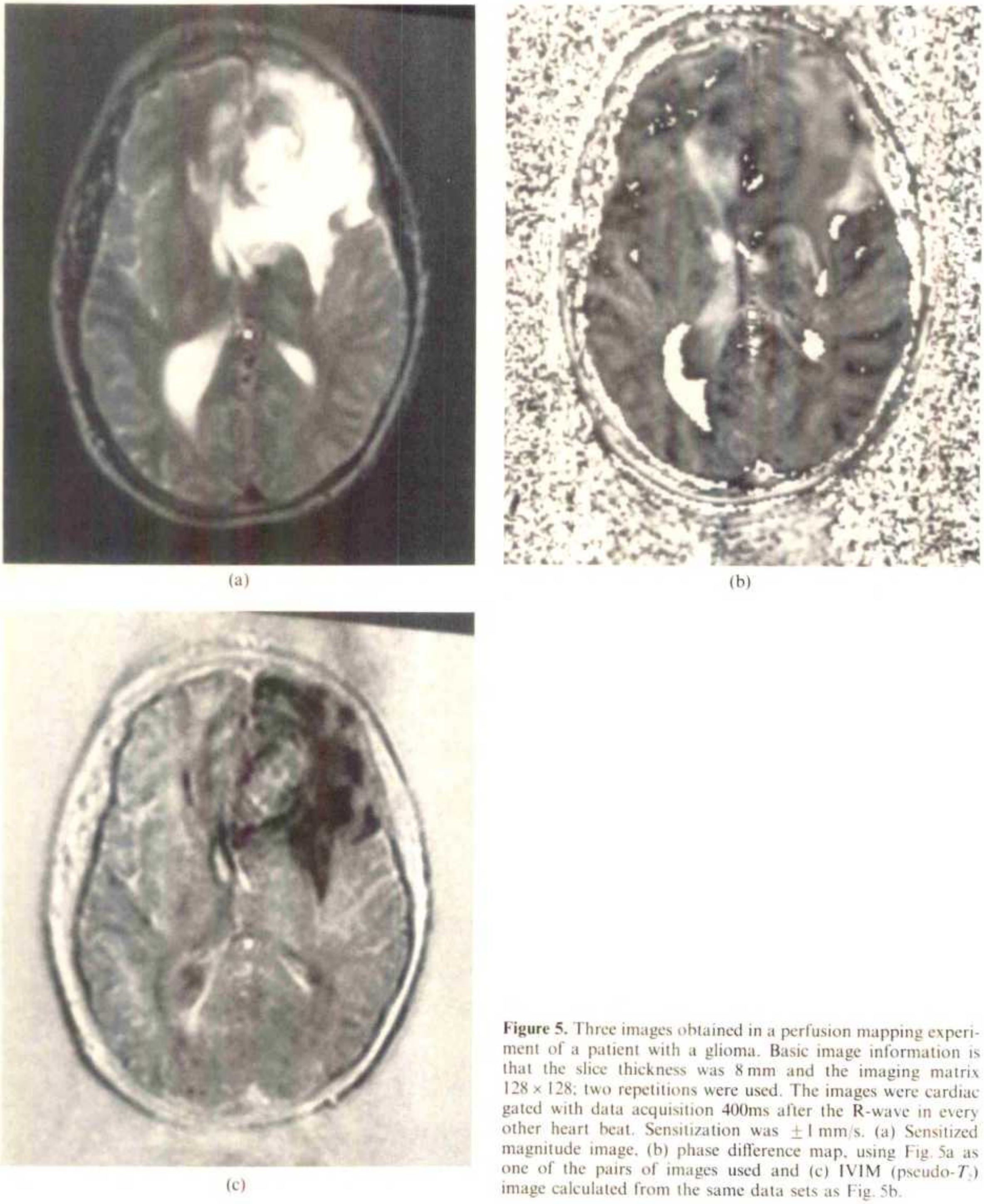


Figure 5. Three images obtained in a perfusion mapping experiment of a patient with a glioma. Basic image information is that the slice thickness was 8 mm and the imaging matrix 128 × 128; two repetitions were used. The images were cardiac gated with data acquisition 400ms after the R-wave in every other heart beat. Sensitization was ±1 mm/s. (a) Sensitized magnitude image, (b) phase difference map, using Fig. 5a as one of the pairs of images used and (c) IVIM (pseudo-T_2) image calculated from the same data sets as Fig. 5b.

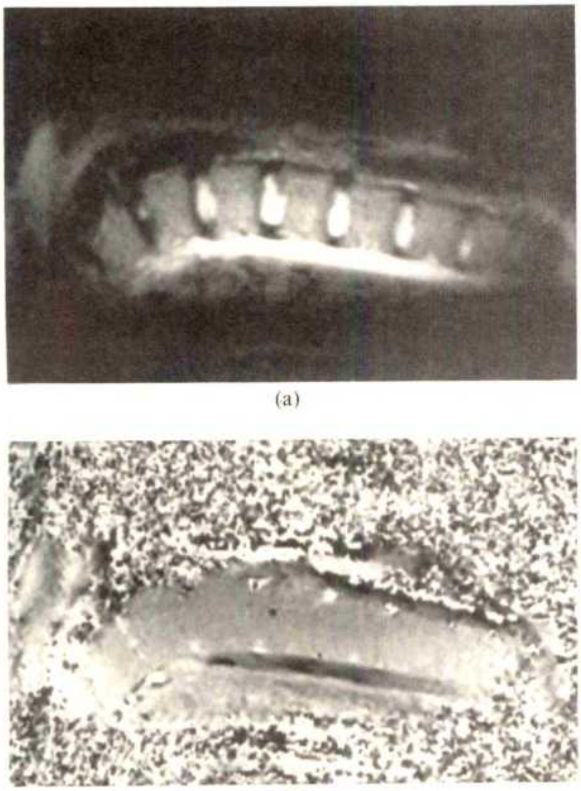


Figure 6. Perfused flow observation in the lumbar spine. Only a small region (slice thickness in the coronal duration 8 mm, in the sagittal one 80 mm) was observed, using otherwise similar parameters to those in Fig. 5, so as to minimize artefact problems from anterior abdominal motion. (a) Magnitude reconstruction of the sensitized data acquired from a patient and (b) phase difference map reconstructed using the data in Fig. 6a as one of the data sets.

methods, groups such as those at the National Heart Hospital have demonstrated details of flow patterns *in vivo* that previously could only be projected theoretically or detected by invasive methods such as catheters. Regardless of anything else, magnetic resonance imaging (MRI) has shown itself to be a research tool of unmatched capability for such work, capable of investigations far beyond the technical scope of, for example, Doppler ultrasound.

Measurement of slow flows

The techniques described above for fast-flow measurement are, in principle, as readily applied to slow flows simply by increasing the degree of sensitization that is used. The only practical limitations appear to be in the timing of the gradient pulses and their durations, and in the central nervous system, where on the whole the spin–spin relaxation time constants (T_2) are quite long, it seems that very high sensitivites can be projected. In practice, the ultimate limitation seems to be imposed by patient motion, both voluntary and involuntary.

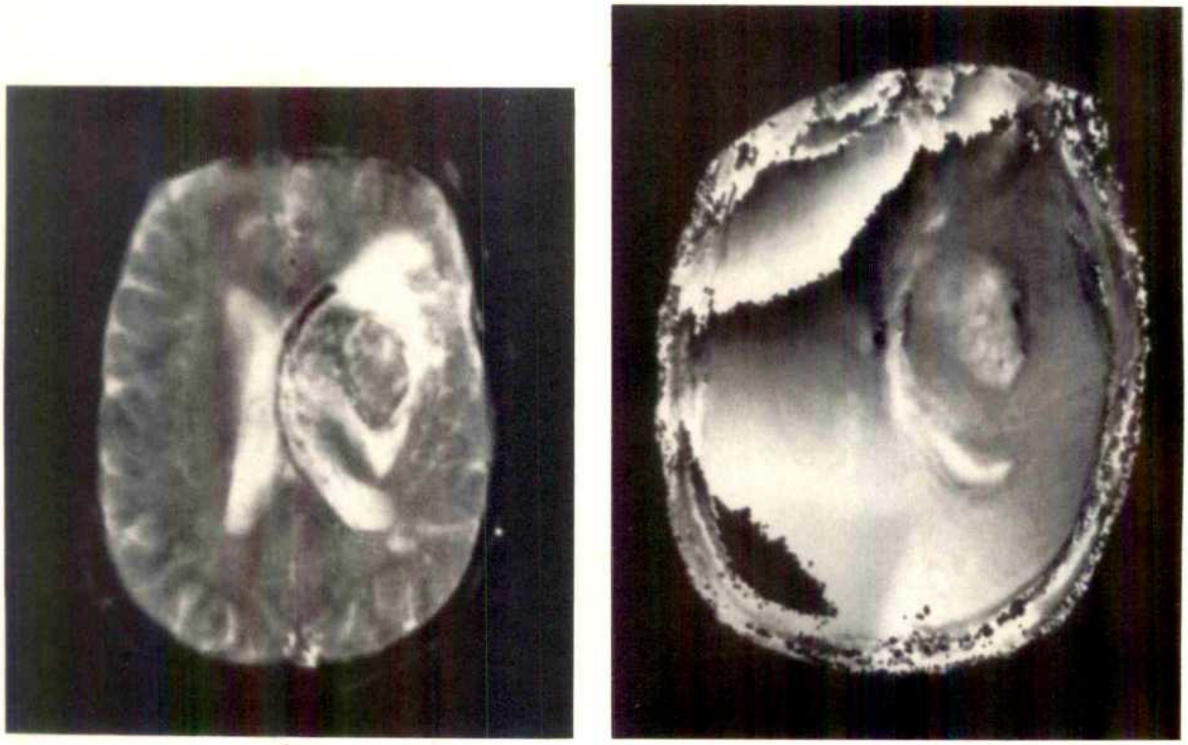
Work on flow in the central nervous system began with studies of CSF flow (Bradley et al, 1986; Sherman & Cohen, 1986), and now includes direct observation of perfused flow. Perfusion is more complex to monitor since most of the signal from the regions of interest arises from protons that are exchanging and moving only over microscopic distances, giving rise to a source of signal decay that is a function of the diffusion coefficient. However, the signals from protons in the blood moving macroscopically through tissue are observable and two effects have been reported. The first is the sort of phase change described previously, observed from bulk net motion along the sensitized direction [intravoxel coherent motion (IVCM) (Young et al, 1988a)] and the second is a mix of dephasing due to coherent motion and other macroscopic flows and the diffusion process, displayed after a calculation similar to that used in arriving at a map of T_2, and called intravoxel incoherent motion (IVIM) (Le Bihan et al, 1986). Figure 5 shows three images: a sensitized image (with a full scale sensitivity to flow of ±1 mm/s; Fig. 5a), the corresponding phase map in Fig. 5b and the associated IVIM image in Fig. 5c. The patient had a glioma in the right frontal lobe, and it is remarkable just how different is the data content of the latter two images. These complex flow patterns seem to be something observed uniquely by MR and, though their meaning is obscure as yet they offer much potential for future work. (Note: the phase maps show velocity, with positive and negative flows showing up light or dark against the mid-shade grey, which corresponds to zero flow. The mottled appearance round the outside arises where the computer calculates the (random) phase differences of the noise in the background.)

Perfusion studies are possible in many body tissues and have been used, for example, in the lumbar spine with sensitization in the antero-posterior direction. Small sections only are excited, to avoid problems with motion in the lower abdomen, and hence the appearance of the images in Fig. 6 where Fig. 6a is the flow sensitized magnitude image and Fig. 6b the phase map. The patient had lower back pain syndrome, and the bright spots showing the presence of higher flow seem to be associated with the condition.

Other regions that have been studied to observe perfused flow are the limbs and the abdomen.

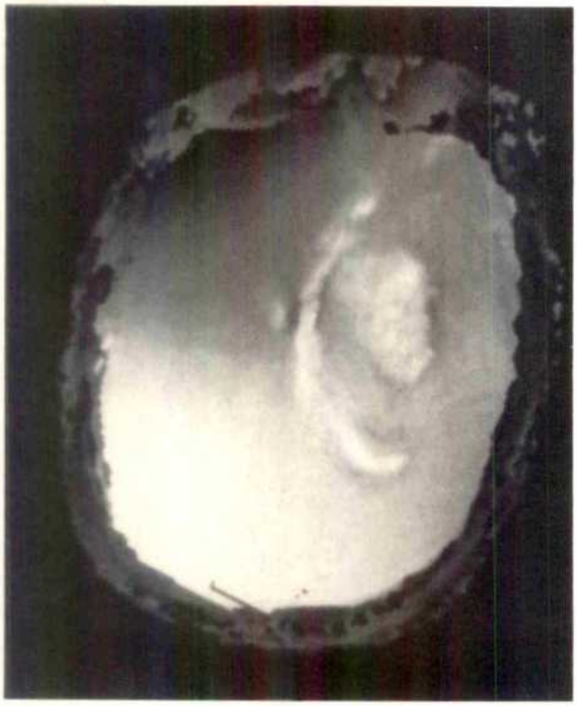
Susceptibility mapping

Field variation mapping is another topic that uses the same sort of phase monitoring techniques as flow measurement. It began, in clinical and biological terms, as an endeavour to find out why it was possible to get much better spectra from some tumours than others in an animal model system. Field mapping, in which the phase differences are calculated between two gradient recalled echo sequences (in one of which data acquisition is delayed relative to that in the other) (Hutchison et al, 1980) suggested that in some tumours haemor-



(b)

(c)



(a)

Figure 7. Results from a susceptibility mapping experiment. Image matrix was 128 × 128, slice thickness 6 mm and two acquisitions of each line of data were obtained with a TR of 1500 ms. (a) Delayed gradient recalled image (magnitude reconstruction) with an effective echo time (TE) of 200 ms; t_D 160 ms. (b) Uncorrected phase difference map, with a sensitivity of ± 0.49 ppm (for one sawtooth cycle). (c) Same image as in Fig. 7b, computer corrected for main field inhomogeneity artefacts.

rhagic tissue was degrading the local field, so inhibiting adequately good shimming of the region of interest (Cox et al, 1987).

The theoretical relationship is, as in the flow case, simple. The phase difference (ϕ) relative to that observed at a reference point (taken to have zero phase difference) is given by:

$$\phi = \gamma \delta B_0 t_D$$

where t_D is the relative time delay between the excitation and data acquisition time of the two sequences and δB_0 is the field deviation relative to that at the reference. Effects due to haemorrhage should not exceed more than about 1 ppm, so that the dominant appearance of most of such maps is determined by main field inhomogeneities. These, however, have a low spatial frequency, much greater than even spectroscopic voxels in dimension, and it is the field variations over voxel dimensions that matter in both imaging and spectroscopy. Changes associated with pathology are usually of short spatial duration. This is illustrated in Fig. 7, which shows a magnitude reconstruction of a delayed gradient recalled echo image (Fig. 7a), the field map obtained using it as one of the images of the pair needed (Fig. 7b) and the phase map resulting after computer correction for main field artefacts (Fig. 7c). The form of the lesion and the field map are noticeably different. This reflects the fact that there are two processes at work, one of which affects the magnitude of the signals from a voxel, the other its phase (both of which can occur together or separately) (Young et al, 1989).

An important factor is the impact these effects have on spectroscopic results since local field perturbations from haemorrhagic tissue can spoil the best shimmed main fields. The impact of the two forms of field degradation on spectra can differ. The first, a phase shift effect as shown in Fig. 7b, results in incorrect chemical shifts, can introduce incorrect splitting of spectral lines and lead to errors in peak assignment and pH, as well as a failure to suppress the normally totally dominant water peak in proton spectroscopy to the degree intended. The other effect, which results in a reduced effective value of T_2 (known as T_2^*) and so rapid extra dephasing of signals, results in poorer, noisier spectra with broad, badly resolved lines.

As has been shown in quite substantial studies of the brain, the two effects are largely uncorrelated and pose a significant threat to spectral quality in about half of tumour, trauma and paediatric examinations (Young et al, 1989).

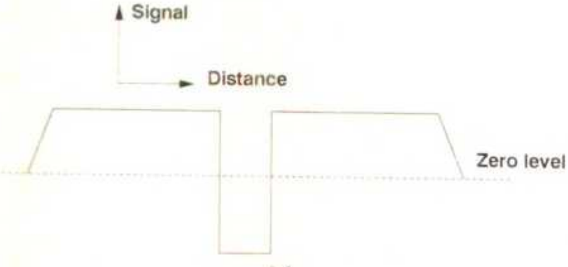
Spectroscopy

Though it may at first sight seem that spectroscopy is remote from other *in vivo* MR strategies and has been enveloped in a mystique all of its own, there is every justification for regarding it as no more than a specialist facet of imaging and not at all far removed from the mainstream. The data may look different and its interpretation seem to be remote from conventional *in vivo* MRI, but the problems faced and the solutions needed for satisfactory results are much more similar than they are different.

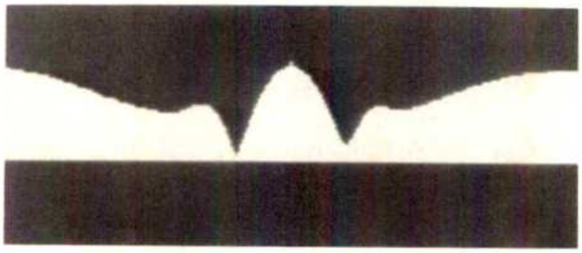
Thus, the starting point is the patient and how he or she is handled. Associated with the patient are a number of common factors regardless of procedures to be undertaken. Even assuming there are no other pressures on time, the patient will only tolerate an examination of limited duration. He or she will move, either voluntarily (for which restraint may be practicable) or involuntarily. (Ideally, the patient's heart will move and blood circulate, and he or she will breathe.) However, because sensitivity is so very low (as has been pointed out already), time and motion will not be avoidable problems. Thus, the patient will need to be made comfortable and awkward and intrusive bits of apparatus and procedures will have to be avoided. Examinations will have to be planned to minimize the risks of its termination and ensure something useful is achieved even if it has to be aborted early on. In the face of all these difficulties, it is comforting to know that the anatomical structures and symmetries are the same as in any other examination. What are not options are the highly invasive and prolonged studies that can be performed using sophisticated support systems on animals or perfused tissues, and which can, without proper interpretation, deliver an unrealistically optimistic view of the possibilities of spectroscopy.

This is even more true when it is considered that, to a significant extent, the animal models that have been developed must now be questioned as to their relevance. The first major failure, now widely recognized, is the suggestion that tumours are acidic. Radda's group at Oxford recognized the incorrectness of this premise early on in their work on whole bodies (Oberhaensli et al, 1986) and others now have confirmed it. Less recognized, as yet, is the failure of the animal systems evaluated using phosphorus-31 spectroscopy to throw extensive light on the phosphomonoester (PME) region of the spectrum. Differences in PME peak amplitudes and relaxation time constants and their variation during therapy are the most significant current observations in *in vivo* phosphorus-31 studies. However, exactly what PME is and whether it is one metabolite, or a series of different ones has not been adequately resolved from the previous work; little more data exists about the neighbouring diester region (PDE).

Thus, in evaluating key regions of the spectra, the observer is forced back onto the radiological basis of looking for changes between normal and abnormal regions, seeking previously evaluated patterns and looking at appearances with a healthy scepticism about numerical values. Observations of this kind apply to other nuclei as well. *In vivo* proton spectroscopy is at the stage of noting that some spectral lines seem to decrease in amplitude relative to those in adjacent normal tissue, while others can increase, remain the same, and, quite often, vary from case to case. Spectroscopy of other nuclei (carbon 13, fluorine 19 particularly of introduced agents such as the chemotherapeutic 5-fluorouracil), though currently being actively studied, has, arguably,



(a)



(b)

Figure 8. Figure to illustrate the artefacts in the formation of a region of interest. Figure 8a shows the ideal profile after one of the inversions in the ISIS technique. Figure 8b is a section through the region of interest, with signal amplitude plotted against displacement. Since this is a magnitude representation, the central spike, which is actually of negative magnetization, appears in the same sense as the rest of the data, and should therefore approximate the shape in Fig. 8a.

not even advanced to the stage where such a point can be made about it.

Connections between imaging and spectroscopic techniques and problems are also far more complex and extensive than is generally perceived. It is conventional wisdom that images are useful to locate spectroscopic regions of interest; many machines have the facility to mark a region on an image, and, superficially, to imply that the resultant data are an uncontaminated representation of signals from metabolites in the place so-defined.

This is a sad simplification, for a whole host of reasons better recognized by imagers than spectroscopists. First, coil characteristics alter unless image and spectrum are collected from the same nucleus, so that, particularly with surface coils, sensitivity profiles seemingly established from a proton image acquired with a double-tuned coil can be quite different in recovering data for a phosphorus spectrum. Secondly, many techniques suffer from complex regions of interest formation artefacts analogous to those encountered in imaging (Young et al, 1988b). Figure 8 shows the target profile for one stage in the acquisition of a localized spectrum using the ISIS method (Ordidge et al, 1986) compared with typical reality, while Fig. 9 shows the amplitude modulation of the region of interest produced by a stimulated echo technique used in proton spectroscopy (Frahm et al, 1988). The region should have a regular rectangular profile and again the reality is very different. Even the quasi-imaging phase encoding methods (Brown et al, 1982; Bailes et al, 1987, 1988), which do produce data covering whole regions of the body, suffer different but equally serious deficiencies. The problem here is that the matrices that can be used, because of the long relaxation time constants of many metabolites and the consequent need for extended data acquisition times, are of very low resolution ($8 \times 8 \times 8$ to $8 \times 8 \times 16$) though, even then, taking 30 min or so for the acquisition of a single data set. When such small data arrays are filtered and discretely Fourier transformed, Gibbs ringing and data smearing result, meaning that the data assigned to one voxel are in fact derived from a mix of signals from it and its neighbours. This is illustrated in Fig. 10 where a single plane of data from an $8 \times 8 \times 8$ matrix set of spectra from a paediatric brain (voxel size 30 mm × 30 mm × 30 mm) is limited. The "bleeding" of data beyond the extent of the brain outline in Fig. 10a is limited. In Fig. 10b, however, which shows localized spectra from a phantom with two cells containing metabolites, the smearing out of data due to filtering is very apparent when it is introduced.

Nevertheless, this sort of chemical shift imaging is the basis of a radiological approach to spectroscopy, allowing direct comparison of involved and uninvolved regions of tissue.

Imaging data, too, can contribute much about the likely quality and integrity of spectral data. Susceptibility effects have already been noted as affecting spectroscopy results. Accuracy of chemical shifts (and, so, measurement of pH, for example) and quality of

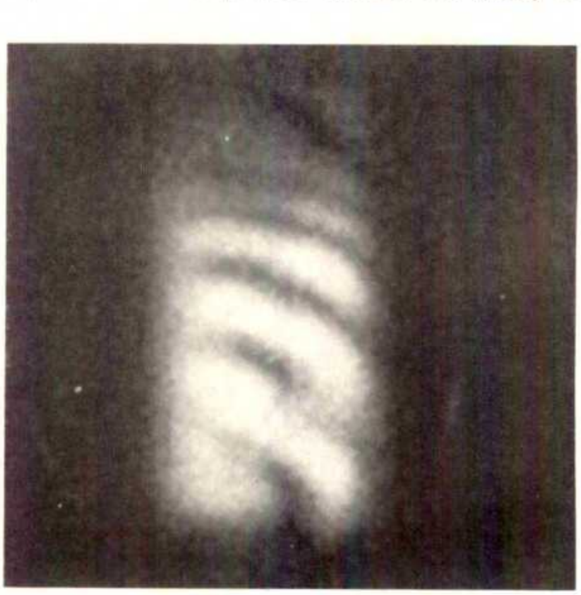


Figure 9. Section of the magnetization in a very well shimmed region of interest (30 mm × 50 mm) formed using the stimulated echo method for proton spectroscopy (Frahm et al, 1988). Even though very well shimmed indeed, an amplitude modulation of around 5% of what should be a very homogeneous region is apparent.

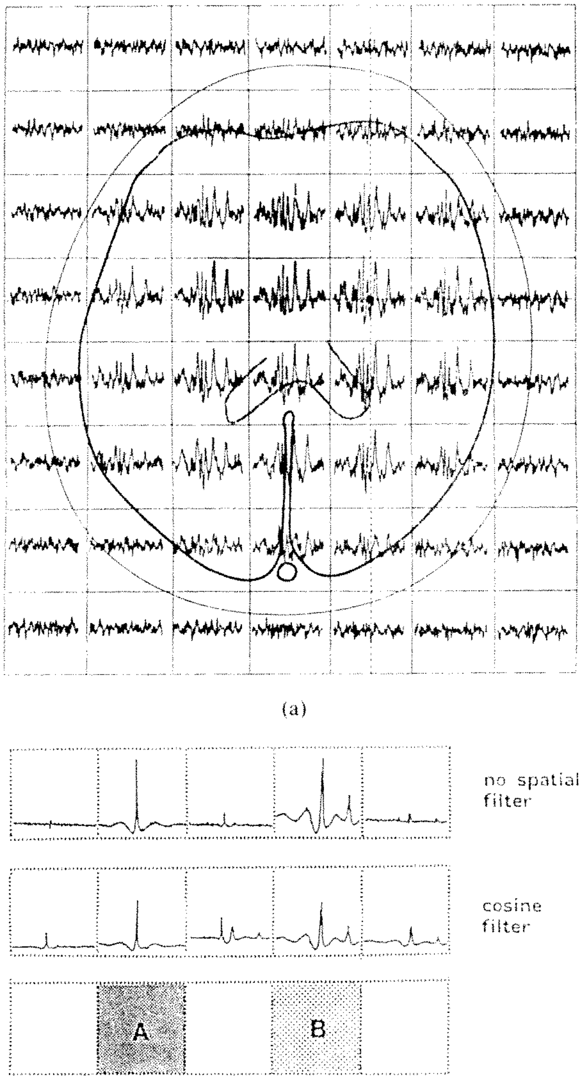


Figure 10. (a) Single plane of spectra (out of eight) from an 8 × 8 × 8 set acquired with a spatial resolution of 30 mm × 30 mm × 30 mm involving 1024 data acquisitions with a TR of 1 s; 1024 acquisitions were obtained in 17 minutes. The r.f. pulse was 500 μs long, phase encoding period 2.5 ms and the time of the start of data acquisition from the middle of the r.f. pulse was 3.1 ms. Data acquisition lasted 200 ms. "Bleeding" of signals outside the head is limited. (b) Effect of filtering in a situation where spectra are acquired from a phantom containing two cells. The "bleeding" of signals in the filtered example is much worse.

suppression of the water peak in proton spectroscopy are affected by the degree of field offsetting that occurs as a result of paramagnetic components from haemoglobin breakdown products. Dephasing owing to the same artefacts results in degraded spectra.

Figure 11 shows one problem. It is a single line from the set of spectra obtained from the knee of a patient with an osteosarcoma prior to therapy, and shows a splitting of the large PCr peak (which should be a single line). While this could be due to a number of things, the phase map of the field showed a complex of variations, so this is a quite likely cause in this case.

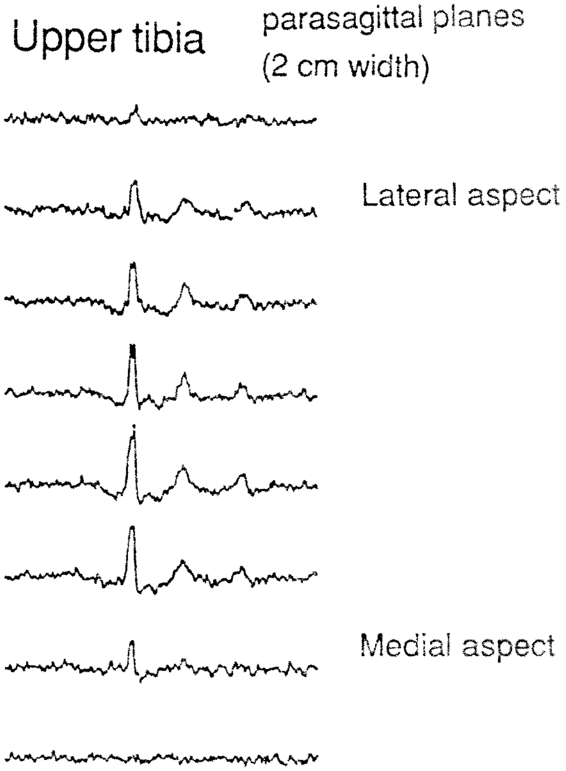


Figure 11. Set of spectra (eight from one line of a plane, which is in turn part of a three-dimensional data set as described in the caption of Fig. 10a). Note the splitting of the large phosphocreatine (PCr) peak thought to be due to susceptibility artefacts.

Spectroscopic studies are also complicated by variations in time constants, reminiscent of those found in imaging but of less certain cause, since they may not just reflect changes in the local environment of normal molecules but the fact that some or all of the nuclei detected in the line could be in a different metabolite from that normally found. This is an aspect of the problem mentioned before in connection with animal models.

Motion artefacts also affect spectra. Imagers are all too familiar with the effects of uncontrolled motion on their results, particularly in the abdomen. Spectroscopists are usually blissfully unaware that they are suffering from them at all. The reason is that they appear in spectra as a degradation of SNR rather than anything else. Again a quasi-imaging approach offers a much better insight into what is happening than a more conventional approach.

Spectroscopy has thus not just its own artefacts of

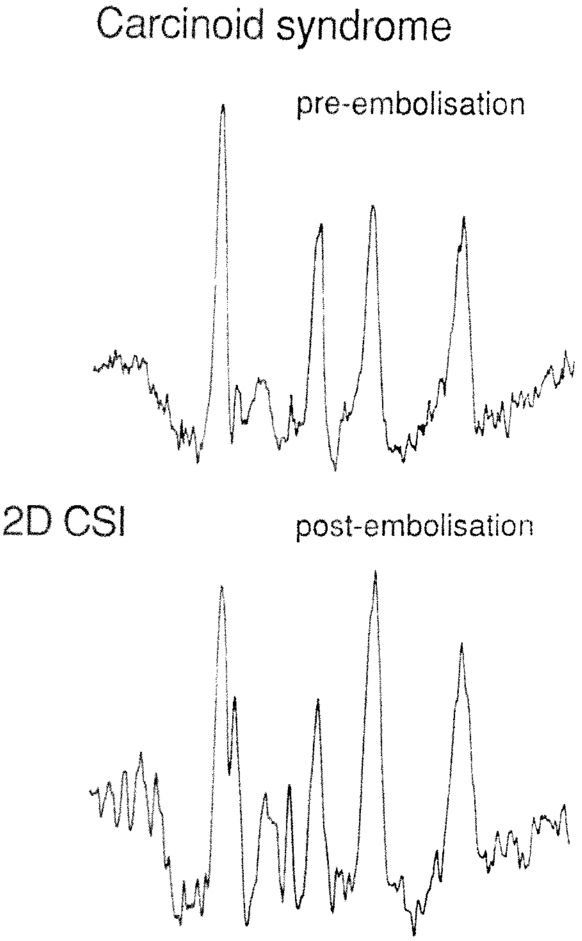


Figure 12. Pair of spectra, part of three-dimensional sets as described in Fig. 10a, prior to and post-embolization in the liver of a patient with a carcinoid tumour. The substantial differences in the spectra are not uncommon, but do not reflect the response of tumours in general.

formation but also those of imaging and it is not surprising that it is evolving strategies that seem more and more like those of the more widespread technique. Just as many imaging strategies involve observing the changes consequent on the injection of contrast media, so does much of spectroscopy revolve around the observation of changes from injected agents, sometimes of real clinical impact in terms of assessing response (*e.g.* the fluorine-19 spectroscopy of 5-fluorouracil; Wolf et al, 1988). The most obvious interest is in the response to therapy generally (Semmler et al, 1987; Gademann et al, 1988) (as illustrated in the pre- and post-embolization of the carcinoid liver of which the spectra are shown in Fig. 12) and, particularly, the hope that changes will be shown earlier spectroscopically than with any other modality, though it is much too early to say whether or not this will prove to be true. If the hope is realized, then we can expect that spectroscopy will find a substantial niche in clinical practice. When it does, even if it is associated more with therapy than anything else, it is reasonable to suggest that the techniques of its operation and the concepts underlying its understanding and thus the logical home for its siting, will be found in radiological units rather than elsewhere.

Conclusion

From the literature, as from direct experience, it is clear that MRI is already recognized as being the modality of preference for a vast range of clinical investigations, in spite of its disadvantages of slow speed and high cost. This paper has attempted to show that it has the potential to do much more. The limitations will always remain, but within their constraints it is to be expected that MR will permit functional studies of patients to a level of sophistication as yet undreamt of.

There will always be things that will be beyond it: detecting anything directly at concentrations of less than ~0.1 mmol, for example. Nevertheless, employing the innovative use of stimulation of a variety of kinds, a vast range of additional non-invasive studies should prove possible. Moreover, the clinical application of spectroscopy looks much closer than it used to, particularly of the hydrogen and fluorine nuclei as present results show (Segebarth et al, 1988; Wolf et al, 1988) while progress is being made in the use of phosphorus in various new directions, most notably in monitoring rejection of transplanted hearts (Herfkens et al, 1988).

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References

ACR, 1983. *American College of Radiology Glossary of NMR Terms* (ACR, Chicago).

Bailes, D. R., Bryant, D. J., Bydder, G. M., Case, H. A., Collins, A. G., Cox, I. J., Evans, P. E., Harman, R. R., Hall, A. S., Khenia, S., McArthur, P., Oliver, A., Rose, M. R., Ross, B. D. & Young, I. R., 1987. Localized phosphorus-31 NMR spectroscopy of normal and pathological human organs *in vivo* using phase-encoding techniques. *Journal of Magnetic Resonance*, *74*, 158–170.

Bailes, D. R., Bryant, D. J., Case, H. A., Collins, A. G., Cox, I. J., Hall, A. S., Harman, R. R., Khenia, S., McArthur, P., Ross, B. D. & Young, I. R., 1988. *In vivo* implementation of three-dimensioinal phase encoded spectroscopy with a correction for field inhomogeneity. *Journal of Magnetic Resonance*, *77*, 460–470.

Bailes, D. R., Gilderdale, D. J., Bydder, G. M., Collins, A. G. & Firmin, D. N., 1985. Respiratory ordered phase encoding (ROPE): a method for reducing respiratory motion artifact in magnetic resonance imaging. *Journal of Computer Assisted Tomography*, *9*, 838–839.

Bates, T. E., Williams, J. R., Busza, A. L., Gadian, D. G. & Procter, E., 1988. A 31P nuclear magnetic resonance study *in vivo* of metabolic abnormalities in rats with acute liver failure. *NMR in Medicine*, *1*, 67–73.

Bradley, W. G., 1984. Factors determining the appearance of flowing blood on NMR images. *Magnetic Resonance in Medicine, 1,* 116 (abstract).

Bradley, W. G., Kortman, K. E., Burgoyne, B., 1986. Flowing cerebrospinal fluid in normal and hychocephalic states. *Radiology, 159,* 611–615.

Brown, T. R., Kincaid, B. M. & Ugurbil, K., 1982. NMR chemical shift imaging in three dimensions. *Proceedings of the National Academy of Science USA, 79,* 3523.

Bryant, D. J., Payne, J. A., Firmin, D. N. & Longmore, D. B., 1984. Measurement of flow with NMR imaging using a gradient pulse and phase difference technique. *Journal of Computer Assisted Tomography, 8,* 588–593.

Bydder, G. M. & Young, I. R., 1985. MRI: clinical use of the inversion recovery sequence. *Journal of Computer Assisted Tomography, 9,* 659–675.

Cox, I. J., Bryant, D. J., Ross, B. D., Young, I. R., Gadian, D. G., Bydder, G. M., Williams, S. R., Busza, A. L. & Bates, T. E., 1987. Spectral resolution in clinical magnetic resonance spectroscopy. *Magnetic Resonance in Medicine, 5,* 186–190.

Crooks, L. E. & Kaufman, L., 1984. NMR imaging of blood flow. *British Medical Bulletin, 40,* 167–169.

Dumoulin, C. L., Souza, S. P., Walker, M. F. & Yoshitomo, E., 1988. Time-resolved magnetic resonance angiography. *Magnetic Resonance in Medicine, 6,* 275–287.

Frahm, J., Gyngell, M. L., Bruhn, H., Merboldt, K. D., Hänicke, W. & Sauter, R., 1988. Localized proton spectroscopy and cerebral metablism in man: new results using stimulated echoes. *Proceedings of the 7th Annual Meeting of the Society of Magnetic Resonance in Medicine, 613.*

Gademann, G., Semmler, W., Bachert-Baumann, P., Gückel, F., Zabel, H.-J., Lenarz, T. & van Kaick, C., 1988. 31PMR spectroscopy and 1HMR tomography in cervical lymphnode metasteses under chemotherapy in short-term follow-up studies. *Proceedings of the 7th Annual Meeting of the Society of Magnetic Resonance in Medicine,* 715.

Herfkens, R. J., Charles, H. C., Negro-Vilar, R. & Van Tright, P., 1988. *In vivo* P-31 spectroscopy of human heart transplants. *Radiology, 169(P),* 179.

Hore, P. J., 1983. Solvent suppression in Fourier transform nuclear magnetic resonance. *Journal of Magnetic Resonance, 55,* 283–300.

Hutchison, J. M. S., Edelstein, W. A. & Johnson, G., 1980. A whole body NMR imaging machine. *Journal of Physics E: Scientific Instruments, 13,* 947–955.

Le Bihan, D., Breton, E., Lallemand, D., Grenier, P., Cabanis, E. & Laval-Jeantet, M., 1986. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurological disorders. *Radiology, 161,* 401–407.

Longmore, D. B., 1986. Theoretical and clinical experience of magnetic resonance in the cardiovascular system. *Syllabus of the Santa Fe NMR Workshop,* 84–91.

Mansfield, P., 1984. Real-time echo-planar imaging. *British Medical Bulletin, 40,* 187–190.

Moran, P. R., 1982. A flow velocity zeugmatographic interleave for NMR imaging in humans, *Magnetic Resonance Imaging, 1,* 197–203.

Mueller, E., Deimling, M. & Reinhardt, E. R., 1985. Quantification of flow phenomena in MRI. *Proceedings of the 4th Annual Meeting of the Society of Magnetic Resonance Medicine,* 587.

Nishimura, D. G., Macovski, A., Pauly, J. M. & Conolly, S. M., 1987. MR angiography by selective inversion recovery. *Magnetic Resonance in Medicine, 4,* 193–202.

Oberhaensli, R. D., Hilton-Jones, D., Bore, P. J., Hands, L. J., Rampling, R. P. & Radda, G. K., 1986. Biochemical investigation of human tumours *in vivo* with phosphorus-31 magnetic resonance spectroscopy. *Lancet, ii,* 8–11.

Ordidge, R. J., Connelly, A. & Lohman, J. A. B., 1986. Image-selected *in vivo* spectroscopy (ISIS). A new technique for spatially selective NMR spectroscopy. *Journal of Magnetic Resonance, 66,* 273–294.

Packer, K. J., 1969. The study of slow coherent molecular motion by pulsed nuclear magnetic resonance. *Molecular Physics, 17,* 355.

Pattany, P. M., Philips, J. J., Chiu, L. C., Lipcamon, J. D., Duerk, J. L., McNally, J. M. & Mohapatra, S. N., 1987. Motion artifact suppression technique (MAST) for MR imaging. *Journal of Computer Assisted Tomography, 11,* 369–377.

Segebarth, C., den Hollander, J. A., Baleriaux, D. & Luyten, P. R., 1988. Metabolic differentiation of human brain tumours with *in vivo* H-1 MR spectroscopy. *Radiology, 169(P),* 84.

Semmler, W., Gademann, G., Bachert-Baumann, P., Zabel, H.-J., Lorenz, W. L. & van Kaick, G., 1987. *In vivo* P-31 study of the response of human tumours to chemotherapy. *Radiology, 165(P),* 360.

Sherman, J. L. & Cohen, C. M., 1986. Magnetic resonance demonstration of normal CSF flow. *Annual Journal of Neuroradiology, 7,* 3–6.

Singer, J. R., 1959. Blood flow measurements by NMR of the intact body. *Science, 130,* 1652–1653.

Stark, D. D., Hendrick, R. E., Hahn, P. F. & Ferrucci, J. T., 1987. Motion artifact reduction with fast spin-echo imaging. *Radiology, 164,* 183–191.

Wolf, W., Presant, C. A., Albright, M. J., Sorris, K. L., Banker, P., Ring, III, R., El Taptassy, A., Atkinson, D. & King, M. E., 1988. F-19 MR spectroscopy of 5-Fu as a method for non-invasive monitoring of drug targeting and delivery. *Radiology, 169(P),* 84.

Young, I. R., 1987. Phase-dependent techniques offer new direction in MRI. *Diagnostic Imaging, August,* 119–131.

Young, I. R., Bailes, D. R., Burl, M., Collins, A. G., Smith, D. T., NcDonnell, M., Orr, J. S., Banks, L. M., Bydder, G. M., Greenspan, R. H. & Steiner, R. E., 1982a. Initial clinical evaluation of a whole body NMR tomograph. *Journal of Computer Assisted Tomography, 6,* 1–18.

Young, I. R., Bailes, D. R., Collins, A. G. & Gilderdale, D. J., 1982b. Image options in NMR. In *NMR Imaging,* ed. by R. L. Witcofski, N. Karsteadt & C. L. Partain (Bowman Gray School of Medicine, Winston-Salem, NC), pp. 15–23.

Young, I. R., Bryant, D. J., Hall, A. S. & Collins, A. G., 1988b. Slice shape artefacts due to selective excitation when the last rf pulse in the sequence is a 90° one. *Proceedings of the 7th Annual Meeting of the Society of Magnetic Resonance in Medicine,* 704.

Young, I. R., Bryant, D. J. & Payne, J. A., 1985. Variations in slice shape and absorption as artifacts in the determination of tissue parameters in NMR imaging. *Magnetic Resonance in Medicine, 2,* 355–389.

Young, I. R., Bydder, G. M., Khenia, S. & Collins, A. G., 1989. Assessment of phase and amplitude effects due to susceptibility variations in magnetic resonance imaging of the brain. *Journal of Computer Assisted Tomography,* 13, 490–494.

Young, I. R., Hall, A. S., Bryant, D. J., Thomas, D. G. T., Gill, S. S., Dubowitz, M. S., Cowan, F., Pennock, J. M. & Bydder, G. M., (1988a). Assessment of brain perfusion with MR imaging. *Journal of Computer Assisted Tomography, 12,* 721–727.

1990, *The British Journal of Radiology*, *63*, 14–18

Testing a policy for skull radiography (and admission) following mild head injury

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Abstract. There has been, and continues to be, conflicting advice regarding skull radiography following an apparently uncomplicated head injury. Policies on admission are often ill defined. In 1983, representatives of the Royal College of Radiologists met neurosurgeons at a seminar in Harrogate organized by the DHSS and laid down clear, but little publicized, joint recommendations: "The Harrogate Criteria". The survey described here evaluated an existing liberal policy for skull radiography (and a loose policy for admissions) against these recommendations, and it was concluded that the number of patients having skull radiography (74% of head injury attenders) was excessive. Measured against the "Harrogate Criteria", requests for 36% of the adult and 47% of children's skull radiographs did not fulfil these criteria. As a corollary, it was also concluded that loose admissions policies could usefully be altered to comply more closely with the Harrogate recommendations. This would not necessarily reduce the numbers admitted, but would provide casualty officers with a framework on which to base this crucial aspect of clinical decision making, where presently there is often very little structure at all. The authors suggest that all the options have not been fully explored, and that a simple but important alteration to the Harrogate guidelines would provide an even closer link between policy on skull radiography and patient admission. Specifically, most patients who are to be admitted do not need skull radiographs.

Over a million patients attend accident and emergency departments in Britain each year following a head injury. The vast majority are mildly injured and recovery is rapid. Between 60% and 80% have a skull radiograph (Gorman, 1987a).

There continues to be disagreement as to the value of skull radiography despite many assessments (Roberts & Shopfner, 1972; Boulis et al, 1978; Eyes & Evans, 1978; de Lacey et al, 1980, Masters, 1980; Royal College of Radiologists (RCR), 1980; Weston, 1981; Mendelow et al, 1983; RCR Working Party, 1983; Snoeck et al, 1984; Brocklehurst et al, 1987; Gorman, 1987b; Masters et al, 1987). In general, radiologists have criticized the clinical value of existing liberal policies on skull radiography (Eyes & Evans, 1978; RCR Working Party, 1981; Bligh et al, 1983; RCR Working Party 1983; Charny et al, 1987), whereas some neurosurgeons and accident surgeons take an opposite view (Mendelow et al, 1983; Briggs et al, 1984; Gorman, 1987a; Gorman, 1987b).

In 1983, the Department of Health organized a seminar in Harrogate at which neurosurgeons as well as members of the RCR Working Party on patient selection for skull radiography produced a report: "The Management of Acute Head Injury". This gave clear criteria (Table I) for hospital admission as well as for skull radiographic examination (Harrogate, 1983).

We report a survey designed specifically to evaluate whether these criteria (Harrogate, 1983) would reduce or increase the present level of skull radiography and admissions in a large general hospital where the existing practices were liberal.

Patients and methods

All patients attending the Accident and Emergency Department at Northwick Park Hospital between 1 September and 31 October 1985 with an injury to the cranio-facial area were included in the survey. An accident and emergency card recorded sixteen items of information (Fig. 1), and the eight junior casualty officers participating in the survey did not know that the purpose was to assess our admission and radiographic policy. When patients had consumed alcohol, this was recorded only when four or more units had been drunk. During the study our existing policies were continued: the casualty officers were advised to request skull radiography for all patients with either a history of loss of consciousness or what appeared to have been a "significant" blow to the head. We also continued to follow our prevailing guidelines for admission, these being a history of loss of consciousness or any doubt about the wisdom of sending a patient home. Adults were admitted to the Observation Ward within the Casualty Department, children (under fifteen) to a paediatric ward, clinically severe injuries to a surgical ward and those requiring a neurosurgical opinion to a neurosurgical centre. All radiographs were reported by one of the participating radiologists within 12 hours (48 hours at the weekends).

Results

Five hundred and sixty-five consecutive patients attending with a head injury were included. There were

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Table I. The Harrogate Criteria[a]

For skull X-ray

Skull X-ray can be helpful but clinical judgement is necessary, and the following criteria will be refined by further experience. The presence of one or more of the following indicates a need for skull X-ray in patients with a history of recent head injury.

1. Loss of consciousnes or amnesia at any time.
2. Neurological symptoms or signs.
3. Cerebrospinal fluid or blood from the nose or ear.
4. Suspected penetrating injury *or* scalp bruising *or* swelling.
5. Alcohol intoxication.
6. Difficulty in assessing the patient (*e.g.* the young, epilepsy).

Note: simple scalp laceration is *not* a criterion for skull X-ray.

For hospital admission

The presence of one or more of the following:

1. Confusion or any other depression of the level of consciousness at the time of examination.
2. Skull fracture.
3. Neurological signs *or* headache *or* vomiting.
4. Difficulty in assessing a patient, *e.g.* alcohol, the young, epilepsy.
5. Other medical conditions—*e.g.* haemophilia.
6. The patient's social conditions *or* lack of responsible adult or relative.

Note: (a) post-traumatic amnesia with full recovery is *not* an indication for admission.
(b) Patients sent home should be given written instructions about possible complications and appropriate action.

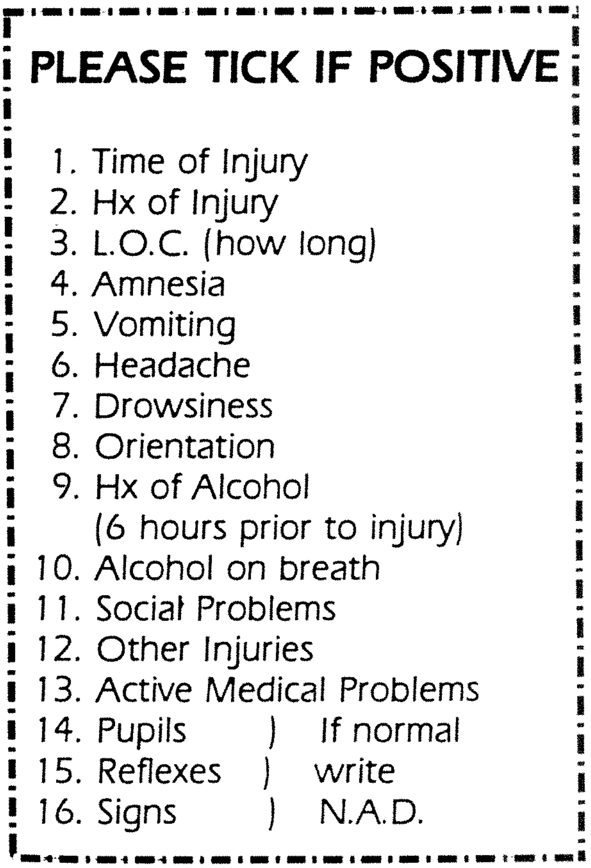
[a] Taken from Harrogate Seminar Report No. 8, DHSS, December 1983.

337 adults (60%) and 228 children (40%). For adults, the mean age was 41 years; 57% were male; 261 (77%) had skull radiographs and 94 (28%) were admitted. For children, the mean age was 6 years, 71% were male, 160 (70%) had skull radiographs and 15 (7%) were admitted.

Skull fractures were present in three adults and one child. Five patients showed symptoms or signs warranting neurological assessment: one adult with a fracture and confusion; one adult without a fracture who was comatose despite resuscitative measures (post-mortem revealed a subarachnoid haemorrhage); two adults with compound fractures and one child with a depressed fracture subsequently elevated. None of the other patients showed evidence of worsening confusion or development of neurological signs. The child with the depressed fracture was initially discharged from Casualty, but recalled the next morning following the positive radiographic report.

The history and clinical findings, the number of patients who had skull radiography, the number admitted and the time of presentation in Casualty are shown in Tables II, III and IV.

Ninety-four adults were admitted and 77 of these (82%) fulfilled the Harrogate Criteria for admission, although 17 of these only conformed to criterion No. 5 ("Other Medical Conditions"). The remaining 17 adults (18% of all adults admitted) did not satisfy any of the Harrogate Criteria. However, 13 of these presented either at a weekend or during unsocial hours (17.00 hours to 09.00 hours). The remaining four were deemed in retrospect to be completely unnecessary admissions. Finally, there were 30 adults who met Harrogate Criteria for admission but who were sent or went home, eight of whom did so against medical advice.



PLEASE TICK IF POSITIVE

1. Time of Injury
2. Hx of Injury
3. L.O.C. (how long)
4. Amnesia
5. Vomiting
6. Headache
7. Drowsiness
8. Orientation
9. Hx of Alcohol
(6 hours prior to injury)
10. Alcohol on breath
11. Social Problems
12. Other Injuries
13. Active Medical Problems
14. Pupils) If normal
15. Reflexes) write
16. Signs) N.A.D.

Figure 1. Questionnaire completed by the casualty officers. (Hx = History; L.O.C. = Loss of consciousness).

Discussion

In 1983, many of the protagonists for and against liberal policies on skull radiography came together and issued clear recommendations for patient admission and for skull radiographic examination. We have chosen to call their guidelines "The Harrogate Criteria".

In this survey, when we applied the Harrogate Criteria first to adults referred for radiography, 36% of skull radiographs were classified as unnecessary. Thus a large reduction in the number of skull examinations could be obtained by abandoning our liberal policy on radiography and adopting the Harrogate Criteria. It is interesting to note that a similar reduction was observed by Clarke and Adams (1987) when they introduced

Table II. History and clinical findings in 565 consecutive head-injury attenders[a]

	All patients				Adults				Children			
	Admitted		Not admitted		Admitted		Not admitted		Admitted		Not admitted	
	Number of patients	%	Number of patients	%	Number of patients	%	Number of patients	%	Number of patients	%	Number of patients	%
Loss of consciousness	63	58	18	4	56	60	15	6	7	47	3	1
Amnesia	50	46	10	2	40	43	7	3	10	67	3	1
Drowsy	28	26	30	7	22	23	10	4	6	40	20	9
Vomiting	18	17	29	6	11	12	11	5	7	47	18	8
Headache	31	28	82	18	26	28	59	24	5	33	23	11
Poor orientation	11	10	11	2	10	11	9	4	1	7	2	1
Alcohol	25	23	29	6	25	27	29	12	0	0	0	0
Other injuries	44	40	211	46	40	43	53	22	4	27	158	74
Unrelated medical problems	24	22	39	9	22	23	27	11	2	13	12	6
Scalp laceration greater than 5 cm	18	17	43	9	18	19	30	12	0	0	13	6
Total number of patients	109		456		94		243		15		213	

[a]Individual patients frequently had two or more of these findings.

guidelines recommended by the RCR (Fowkes et al, 1984). Though we do not in any way criticize those rather different guidelines, we stress that the importance of the Harrogate Criteria is that the recommendations were drawn up by a broad cross-section of specialists, and perhaps should therefore carry particular weight because of the ecumenical composition of that group.

We have considered children as a separate group because the juvenile brain responds very differently to cranial trauma (Masters, 1980). In children, the association of a skull fracture with an intracranial haematoma is much lower (Burkinshaw, 1960; Harwood-Nash et al, 1971; Roberts & Shopfner, 1972). Most children with an intracranial haematoma do not have a skull fracture. Retrospective application of the Harrogate Criteria to the children in this series halved the number of paediatric skull examinations from our present level of 70% of paediatric head injury attenders.

Let us consider the Harrogate Criteria for hospital admission, specifically as they affect adults, who comprise 86% of all patients admitted in this survey. It has been our practice, as is common, to admit routinely for overnight observation all those who have been transiently unconscious. During the 1970s neurosurgeons began to advise against this practice suggesting that patients with normal skull radiographs who were otherwise well should be sent home. In this way a liberal policy on skull radiography would result in savings from reduced admissions (Jennett, 1974). This represented a very real difference between the views of the radiologists who deemed most skull radiographs to be useless and those of the neurosurgeons who wished to use negative skull radiographs to reduce expensive and bed blocking admissions (de Lacey et al, 1980).

In the series presented here, there were 17 adults who did not fulfil the Harrogate Criteria for admission but who were admitted because of loss of consciousness and for no other reason. Loss of consciousness is clearly defined under the Harrogate Criteria as necessitating radiography but not admission. Now that it is accepted

Table III. Attenders who had skull radiography

	Adults		Children	
	Number	%	Number	%
Skull radiography in those admitted	92/94	98	15/15	100
Skull radiography in those not admitted	169/243	70	145/213	68

Table IV. Patients with head injury: time of presentation

Hours	Adults		Children	
	Number of patients	%	Number of patients	%
Monday to Friday				
09.00–16.00	108	32	68	30
16.00–24.00	81	24	87	38
24.00–09.00	39	12	4	2
Weekends	109	32	69	30
Total	337	100	228	100

by British neurosurgeons (Harrogate 1983) that loss of consciousness is no longer a reason for admission but is a reason for radiography, then the logic of using negative skull radiographs to reduce admissions in these patients no longer applies. When we applied the Harrogate Criteria for admission (Table I), we found that 17 patients who were admitted did not fulfil any of them. However, 30 patients who should have been admitted went home. Thus, strict application of the Harrogate Criteria may well increase admissions for observation.

It is important to note that this survey revealed that the decision to admit was often influenced by factors other than a head injury alone and these included alcohol (16% of those admitted), other injuries (28%), unrelated medical problems (15%) and adverse social circumstances (5%). Clearly, a large proportion of our patients who were admitted cannot be classified as "head injuries only". This very important feature needs to be emphasized when comparing our results with those derived from other surveys, for example, those analysing results from head-injured patients admitted to neurosurgical wards. The latter represent a more highly selected, quite different group. Differing patient selection producing apparently discordant results requires particular emphasis, because almost all surveys on skull radiography have usually been followed by vigorous disagreement (Charny et al, 1987; Jennett & Teasdale, 1987; de Lacey & Wignall, 1983).

Indeed, at first sight it does appear that other large surveys have achieved results quite different from ours, in that application of guidelines similar to Harrogate have seemingly reduced, not increased, admissions (Weston, 1981; Gorman, 1985; Fowkes et al, 1986; Brocklehurst et al, 1987). The explanation surely lies in differing patient selection. For example, in the study by Fowkes et al (1986), the authors used data previously collected by the RCR from nine accident departments in the UK and then applied the Harrogate guidelines for admission to this earlier intelligence. Our survey indicates that admissions would be increased by application of the Harrogate guidelines, whereas Fowkes et al (1986) found that admissions would be reduced. However, they were highly selective in their choice of patients, excluding from their analysis those who had "lack of responsible adult to supervise the patient; other social problems", (*i.e.* Harrogate Criterion No. 6, Table I). They also excluded "patients who had other injuries or fractures . . . because we did not wish to include . . . patients who may have been admitted for other injuries". In our survey 28% of the head-injured adults who were admitted had other injuries. Fowkes' patients and those analysed in our survey are markedly different: it is consequently hardly surprising that our results are so disparate. Time and again, differing patient selection has confused discussion of results and implications from head injury surveys.

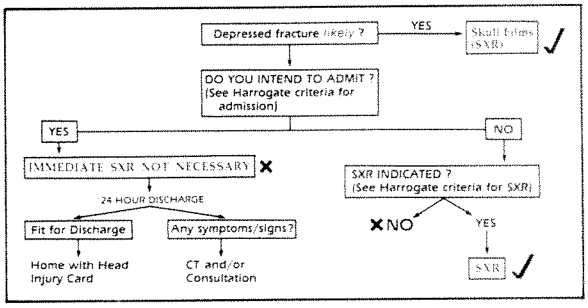

Depressed fracture *likely* ?
YES
Skull films (SXR)
✓
DO YOU INTEND TO ADMIT ? (See Harrogate criteria for admission)
YES
NO
IMMEDIATE SXR NOT NECESSARY
✗
24 HOUR DISCHARGE
Fit for Discharge
Any symptoms/signs?
Home with Head Injury Card
CT and/or Consultation
SXR INDICATED ? (See Harrogate criteria for SXR)
✗NO
YES
SXR
✓

Figure 2. A suggested protocol for skull radiography following an apparently uncomplicated head injury. There is a particular group of patients in whom skull radiography is valuable, *i.e.* those with a depressed fracture (Jennett 1971; Heiskanen et al, 1973).

The primary purpose of this study was to make an assessment of our existing policies on skull radiography and admission compared with the recommendations from Harrogate. Our main conclusion is clear: loose and liberal policies on skull radiography should be abandoned. Large reductions in skull radiography (adults down by 36% and children by 47%) are predicted from adopting the Harrogate guidelines. We recommend too that present loose admission policies should also be abandoned, and that the Harrogate Criteria provide a sensible admissions structure for casualty officers to follow. However, we suggest that a further reduction in the number of skull radiographs could be achieved by an additional sensible integration of policies on admission and skull radiographs. The decision to admit is often taken prior to skull radiography. Those admitted for observation are monitored whilst in hospital, clinically re-assessed before they are discharged and only then, if completely well, are they sent home with a head injury instruction sheet. If adverse symptoms or signs develop at any time whilst they are in hospital then immediate discussion with a neurosurgeon is recommended and computed tomography or transfer to a neurosurgical unit arranged.

It is important to stress this continuing clinical assessment, as it would be a mistake to attempt to replace it by confidence in radiography. Indeed, Bligh (1983) reported that as many as 30% of patients with unrecognized skull fractures are sent home from accident departments. It would thus be a mistake to rely on such an unreliable interpretation of skull radiographs, 68% of which are obtained (from this series) at times when a radiologist is not normally available within the hospital for consultation. Furthermore, we have scrutinized the literature and cannot find a report of a group of patients (as against opinion only) that indicates the risk to those admitted who do have a fracture but no symptoms or signs at "24 hours" (Fig. 2), and yet are subsequently found to have an intracranial haematoma. It is pertinent however, that Masters et al (1987), analysing over 22 000 head-injury attenders, found that of those with a skull fracture, 91% did not have an associated intracranial injury. We therefore propose that those admitted for observation need not have skull radiography at the time of admission for any of the reasons given in the Harrogate Criteria, except when there is cerebrospinal fluid or blood from the nose or ear, a suspected penetrating injury or when a depressed fracture is likely.

Norcross (1987) has properly emphasized that it is imperative to publicize the fact that no system of head-injury care will give complete security against tragic mischance. It should be affirmed also that there is not necessarily one single, good, policy on skull radiography following a head injury. The Harrogate guidelines represent one of several prescriptions which have been promulgated. We suggest that they can still benefit from further modification and Fig. 2 represents a clinically sound protocol which integrates policies on admission and skull radiography for an apparently uncomplicated injury.

References

Bligh, A. S., 1983. The management of acute head injury. In *Harrogate Seminar Report No. 8* (DHSS, London).

Bligh, A. S., Davies, R. H., Evans, W. P., Evans, K. T., Hacking, P. M., Hugh, A. E., Laws, J. W., McNulty, M. R., Oliver, R. M., Roberts, C. J. & Steiner, R. E., 1983. Skull X-ray guidelines. *Lancet 1*, 1164.

Boulis, Z. F., Dick, R., & Barnes, N. R., 1978. Head injuries in children—aetiology symptoms, physical findings and X-ray wastage. *British Journal of Radiology, 51*, 851–854.

Briggs, M., Clarke, P., Crockard, A., Cummins, B., Galbraith, S., Garfield, J., Jeffreys, R., Jennett, B., Kalbag, R., Mendelow, A. D., Miller, J. D., Price, D., Taylor, J., Teasdale, G. & Uttley, D., 1984. Suggestions from a group of neurosurgeons. Guidelines for initial management after head injury in adults. *British Medical Journal, 288*, 983–985.

Brocklehurst, G., Gooding, M. & James, G., 1987. Comprehensive care of patients with head injuries. *British Medical Journal, 294*, 345–347.

Burkinshaw, J., 1960. Head injuries in children. Observations in incidence and causes with an inquiry into the value of routine skull X-rays. *Archives of Disease in Childhood, 35*, 205–214.

Charny, M. C., Ennis, W. P., Evans, K. T. & Roberts, C. J., 1987. Head injuries in the elderly. *British Medical Journal, 294*, 771.

Clarke, J. A. & Adams, J. E., 1987. Skull radiographs after head injury. *Lancet 2*, 457.

de Lacey, G., Guilding, A., Wignall, B., Reidy, J. & Bradbrooke, S., 1980. Mild head injuries: a source of excessive radiography? *Clinical Radiology, 31*, 457–462.

de Lacey, G. & Wignall, B. K., 1983. Head injuries in adults. *British Medical Journal, 287*, 1546.

Eyes, B. & Evans, A. F., 1978. Post-traumatic skull radiographs. Time for a reappraisal. *Lancet 2*, 85–86.

Fowkes, F. G. R., Ennis, W. P., Evans, R. C., Roberts, C. J. & Williams, L. A., 1986. Admission guidelines for head injuries. Variance with clinical practice in accident and emergency units in the UK. *British Journal of Surgery, 73*, 891–893.

Fowkes, F. G. R., Evans, R. C., Williams, L. A., Gehlbach, S. H., Cooke, B. R. B. & Roberts, C. J., 1984. Implementation of guidelines for the use of skull radiographs in patients with head injuries. *Lancet 2*, 795–797.

Gorman, D. F., 1987a. The utility of post traumatic skull X-rays. *Archives of Emergency Medicine, 4*, 141–150.

——1987b. Head injuries in the elderly. *British Medical Journal, 294*, 1159.

——1985. Were you knocked out? Yes, but I wasn't admitted. *Archives of Emergency Medicine, 2*, 121–129.

Harrogate Seminar Report, No. 8, 1983. *The management of acute head injury* (Department of Health and Social Security, London).

Harwood-Nash, D. C., Hendrick, E. B. & Hudson, A. R., 1971. The significance of skull fractures in children. *Radiology, 101*, 151–155.

Heiskanen, O., Martilla, I. & Valtonen, S., 1973. Prognosis of depressed skull fracture. *Acta Chirurgiae Scandinavica, 139*, 605–608.

Jennett, B., 1971. Unnecessary X-rays. *British Medical Journal, 2*, 399.

——1974. Head injuries. *Medicine, 32*, 1873–1884.

Jennett, B. & Teasdale, G., 1987. Head injuries in the elderly. *British Medical Journal, 194*, 1159.

Masters, S. J., 1980. Evaluation of head trauma: efficacy of skull films. *American Journal of Roentgenology, 135*, 539–547.

Masters, S. J., McLean, P., Arcese, J. F., Brown, R. F., Campbell, J. A., Freed, H. A., Heff, G. H, Hoff, J. T., Kobrine, A., Koziol, D. F., Marasco, J. A., Merton, D. F., Metcalfe, H., Morrison, J. L., Rachlin, J. A., Shaver, J. W. & Thornbury, J. R., 1987. Skull X-ray examinations after head trauma. Recommendations by a multidisciplinary panel and validation study. *New England Journal of Medicine, 316*, 84–91.

Mendelow, A. D., Teasdale, G., Jennett, B., Bryden, J., Hessett, C. & Murray, G., 1983. Risks of intracranial haematoma in head injured adults. *British Medical Journal, 287*, 1173–1176.

Norcross, K., 1987. Head injuries. Whither specialization? *Journal of the Royal Society of Medicine, 80*, 58.

Roberts, F. & Shopfner, C. E., 1972. Plain skull roentgenograms in children with head trauma. *American Journal of Roentgenology, 114*, 230–240.

Royal College of Radiologists, 1980. A study of the utilization of skull radiography in nine accident and emergency units in the UK. *Lancet 2*, 1234–1237.

——1981. Costs and benefits of skull radiography for head injury. *Lancet 2*, 791–795.

Royal College of Radiologists Working Party, 1983. Patient selection for skull radiography in uncomplicated head injury; a national study by the Royal College of Radiologists. *Lancet 1*, 115–118.

Snoek, J. W., Minderhoud, J. M. & Wilmink, J. T., 1984. Delayed deterioration following mild head injury in children. *Brain, 107*, 15–36.

Weston, P. A. M., 1981. Admission policy for patients following head injury. *British Journal of Surgery, 68*, 663–664.

1990, *The British Journal of Radiology*, *63*, 19–21

Randomized trial of laser-assisted passage through occluded femoro-popliteal arteries

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Abstract. A randomized trial was carried out in patients with occlusions of the femoro-popliteal artery to compare the passage of metal-tipped optical fibres with guide wires and catheters through the occlusions, prior to balloon angioplasty. The study was in a provincial English teaching hospital providing a vascular service for the area. Fifty patients were entered: 25 into the "laser" group and 25 into the "control" group. End points were (a) the success in passage through the occlusion and (b) the outcome 1 month after passage. Comparison of the groups showed no appreciable difference between the two methods with regard to age, sex, symptoms, incidence of diabetes, or previous myocardial infarctions. Successful passage through the occlusion followed by dilatation was achieved in 18 (72%) patients in the laser group and 20 (80%) in the control group. After 1 month, 13 (52%) arteries in the laser group were patent compared to 13 (57%) in the control group. Confidence limits for the difference in success of passage are −15% to +31%, and −24% to +33% for patency after 1 month. Since these limits include zero, it is unlikely that a longer trial would alter the difference between the two methods. The results suggest that the laser system currently in use is no better than conventional methods.

Experience with balloon angioplasty in lower limb ischaemia has shown that most failures occur in the initial attempt and the succeeding few months (Cole et al, 1987; Murray et al, 1987), with a good prognosis after 1 year. Attempts to improve the initial success rate have included using laser energy to provide a passage through occluded arteries. Initial attempts using bare optical fibres showed a high perforation rate both in animal experiments (Abela et al, 1985) and in humans (Ginsburg et al, 1985; Cumberland et al, 1986a) and metal-capped fibres were then introduced. The metal tip is heated by laser energy and applied directly to the atheromatous lesion. This technique has been claimed to increase the ability to pass through occluded segments safely, and possibly to have an increased long-term success rate (Cumberland et al, 1986b; Sanborn et al, 1988).

We have carried out a randomized trial of laser-assisted angioplasty to compare the passage of metal-tipped optical fibres through occluded femoro-popliteal arteries with that of conventional guide wires and catheters, prior to balloon angioplasty.

Methods and equipment

Patients found at angiography to have occlusions of the superficial femoral artery (SFA) were discussed at a joint radiologico-clinical meeting. Patients with lesions that were clinically and haemodynamically relevant to their symptoms were offered balloon angioplasty after their occlusions had been passed using either a metal-tipped optical fibre (the "laser" group) or a conventional guide wire and catheter (the "control" group). Randomization was based on whether the patients' birth was in an even or an odd year, and this was not known at the time of decision. An 8 F introducer and sheath was positioned antegradely in the SFA, and the occlusion was approached through this with either the laser probe or a catheter over a guide wire (either a van Andel tapered Teflon catheter or a straight 5.5 F polyethylene catheter). Before balloon dilatation, 3000 u Heparin were injected and following the procedure patients were asked to take 150 mg aspirin each day.

An argon laser (Trimedyne) was used for treating the first 32 patients and then a neodymium–YAG laser (Cardiolase). In both cases 10–12 W of laser energy was used to heat the metal tip on the fibre, and there was no significant difference between the successes in the first 32 randomly assigned patients (11 out of 14) and those in the last 18 (7 out of 11). The size of the probe tip was 1.5 mm for the first 30 randomized patients and 2 mm for the remainder; this also made no significant difference. All patients were catheterized by W.D.J. or P.M., both experienced in angioplasty. The trial was approved by the Ethical Committee of the Bristol and Weston Health Authority, and started after experience had been gained in using the laser system in other patients.

Patients

The trial had 50 patients, 25 in each group (Table I). There was no difference between the groups, apart from the increased number of diabetics in the control group (nine compared with four), shorter mean length of occlusions in the control (6.6 cm compared with 8.6 cm) and reduced number of calf vessels in the laser group (mean number patient: 1.5 compared with 1.8). None of

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Table I. Composition of laser and control groups

	Laser	Control
Sex		
Males	13	14
Females	12	11
Total	25	25
Age		
Mean	69.4	70.8
Median	70	71
Range	44–89	47–91
Diabetes	4 (16%)	9 (36%)
Myocardial ischaemia	1 (4%)	3 (12%)
Indication		
Claudication	10 (40%)	11 (44%)
Rest pain or ischaemic change	15 (60%)	14 (56%)
Occlusion site		
SFA	13 (52%)	13 (52%)
SFA Popliteal	12 (48%)	12 (48%)
Length (cm)		
Mean	8.6	6.5
Median	8.0	5.0
Range	3.0–17.0	0.5–24.0
Calcification	4 (16%)	5 (20%)
Arteries in calf		
Mean number patent	1.5	1.8
Patients with:		
≤1	16 (64%)	10 (40%)
2 or 3	9 (36%)	15 (60%)

these differences was statistically significant (Mann–Whitney U-test or χ^2-test, as appropriate).

Results

Success was defined as successful passage through the occlusion followed by balloon dilatation and flow of contrast medium through the lesion into the calf vessels to demonstrate patency. There was successful passage in 20 (80%) control patients and in 18 (72%) patients in the laser group, and after 1 month 13 (57%) of the control group and 13 (52%) of the laser group were patent (Table II).

In two of the five control patients in whom the initial passage was unsuccessful, a metal-tipped optical fibre could be passed through the occlusion. These patients were then excluded from the trial (although they remained patent after 1 month). In none of the seven patients in whom the laser failed could a guide wire and catheter be passed through the occlusion.

There was no significant difference in successful passage or in patency after 1 month between the two groups; the confidence limit for the difference in success was −15% to +31%, and for patency after 1 month was −24% to +33%. There was no significant correlation between failure of the procedure and calcification of the lesion, its length, site or the number of calf vessels present.

Table II. Comparison of results in two groups

	Laser	Control
Passage through lesion		
Number of patients	25	25
Successful passage	18 (72%)	20 (80%)
Complications of attempted passage:		
None	15 (60%)	16 (64%)
Perforation	4 (16%)	2 (8%)
Dissection	1 (4%)	5 (20%)
Thrombosis	5 (20%)	1 (4%)
Spasm	0	1 (4%)
Follow-up after attempted passage[a]		
Number of patients available	25	23
Patent at 48 h	14 (56%)	15 (65%)
Patent at 1 month	13 (52%)	13 (57%)
Operations after 1 month		
None	18 (72%)	19 (76%)
Bypass	2 (8%)	3 (12%)
Amputation of leg	3 (12%)	0
Amputation of toes	1 (4%)	3 (12%)
Sympathectomy	1 (4%)	0

[a] Two patients in the original control group, in whom the occlusion could not be passed, subsequently had a successful laser passage, but have been omitted from this table.

Discussion

Angioplasty has a high success rate in short segmental stenoses (Fleisher et al, 1987), and there seems little point in using an expensive new technique for these lesions. For this reason we included only patients with occluded superficial femoral and popliteal arteries in the trial, and since many SFA lesions are treated in practice by exercise, medication and stopping smoking (Ginsburg, 1988) we have treated only those patients in whom interventional treatment was indicated on clinical and haemodynamic grounds.

The trial has shown no significant difference between the laser and the control group in the ability of either technique to pass through an occlusion or in patency after 1 month. Confidence intervals include zero and although the numbers in each group are relatively small, there are no grounds to suggest that a longer study would change the difference between the two methods. Similar results in the success of passage have been found in an unrandomized study (Levy et al, 1989).

The argon type of laser is expensive to buy and instal (Smithson et al, 1989), and although the newer neodymium–YAG laser that we later used has no installation costs and is considerably more mobile and convenient, its capital cost is approximately £35 000. Metal-tipped optical fibres cost £300 each and can be used only once. Compared with bare fibres they reduce the incidence of perforation, which was still twice that of the control group in this study, but have a higher incidence of immediate thrombosis (20%) than in the control group

(4%). The use of laser energy to heat a metal tip is expensive; other, less costly methods of heating the tip are being explored (Litvack et al, 1987). Newer attempts to use laser energy directly include sapphire probes, which transmit a high proportion of laser light (Lammer & Karnel, 1988) and combined laser and balloon devices, which hold a bare optical fibre centrally in the artery (Nordstrom et al, 1988). Neither of these methods has yet been shown to have any major advantage over the hot-tip optical fibre used here.

In this study the percentage of occlusions not treatable by conventional angioplasty was small. Our current policy for treatment of occluded SFAs is to offer angioplasty initially, and to consider surgical bypass in selected cases. This is because angioplasty is safer, has fewer complications, is less painful and is preferred by patients. Even so, bypass has a patency advantage after 1 month (Cole et al, 1987) and up to 5 years, where bypass patencies of up to 62% have been reported (Michaels, 1989) compared with our angioplasty patency of 53% in femoro-popliteal segments (Cole et al, 1987).

Improvements in both methods of treatment are likely to depend on vigilance in the post-intervention period, when thrombosis and restenosis are common causes of early failure. There will doubtless continue to be advances in laser and related technology, and there remains the hope, so far unrealized, that better recanalization rates will be achieved with reductions in the numbers of early failures. Claims that long-term patency is improved after laser angioplasty will be assessed by longer-term follow-up of the patients in this trial, which has been designed to meet the recommendations for life table analysis (Rutherford, 1986) that all randomized patients should be followed up and included when results are published.

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References

ABELA, G. S., NORMANN, S. J., COHEN, D. M., FRANZINI, D., FELDMAN, R. L., CREA, F., FENECH, A., PEPINE, C. H. & CONTI, C. R., 1985. Laser recanalization of occluded atherosclerotic arteries. An *in vivo* and *in vitro* study. *Circulation, 71*, 405–411.

COLE, S. E. A., BAIRD, R. N., HORROCKS, M. & JEANS, W. D., 1987. The role of balloon angioplasty in the management of lower limb ischaemia. *European Journal of Vascular Surgery, 1*, 61–65.

CUMBERLAND, D. C., TAYLER, D. I. & PROCTER, A. E., 1986a. Laser-assisted percutaneous angioplasty: initial clinical experience in peripheral arteries. *Clinical Radiology, 37*, 423–428.

CUMBERLAND, D. C., TAYLER, D. I., WELSH, C. L., GUBEN, J. K., SANBORN, T. A., MOORE, D. J., GREENFIELD, A. J. & RYAN, T. J., 1986b. Percutaneous laser thermal angioplasty: initial clinical results with a laser probe in total peripheral artery occlusions. *Lancet i*, 1457–1459.

FLEISHER, H. L., THOMPSON, B. W., MCCOWAN, T. C., FERRIS, E. J., REIFSTECK, J. E. & BARNES, R. W., 1987. Human percutaneous laser angioplasty. *American Journal of Surgery, 154*, 666–669.

GINSBURG, R., 1988. Percutaneous laser angioplasty in the treatment of peripheral vascular disease. *Thoracic and Cardiovascular Surgeon, 36, Supplement II*, 142–145.

GINSBURG, R., WEXLER, M., MITCHELL, R. S. & PROFITT, D., 1985. Percutaneous transluminal laser angioplasty for treatment of peripheral vascular disease. *Radiology, 156*, 619–624.

LAMMER, J. & KARNEL, F., 1988. Percutaneous transluminal laser angioplasty with contact probes. *Radiology, 168*, 733–737.

LEVY, J. M., HESSEL, S. J., HORSLEY, W. W., COOK, G. C. & DICKEY, J. E., 1989. Value of laser-assisted angioplasty in the community hospital. *Radiology, 170*, 1017–1018.

LITVACK, F., GRUNDFEST, W., MOHR, F., STRUHL, B. & FORRESTER, J. S., 1987. "Hot-tip" angioplasty by a novel radiofrequency catheter. *Circulation, 76, Supplement IV*, 47.

MICHAELS, J. A., 1989. Choice of material for above-knee femoro-popliteal bypass graft. *British Journal of Surgery, 76*, 7–14.

MURRAY, R. R., HEWES, R. C., WHITE, R. I., MITCHELL, S. E., AUSTER, M., CHANG, R., KADIR, S., KINNISON, M. L. & KAUFMAN, S. L., 1987. Long-segment femoro-popliteal stenoses: is angioplasty a boon or a bust? *Radiology, 162*, 473–476.

NORDSTROM, L. A., CASTANEDA-ZUNIGA, W. R., YOUNG, E. G. & VON SEGGERN, K. B., 1988. Direct argon laser exposure for recanalization of peripheral arteries: early results. *Radiology, 168*, 359–364.

RUTHERFORD, R. B. (Chairman), 1986. *Ad Hoc* Committee on Reporting Standards. Suggested standards for reports dealing with lower extremity ischemia. *Journal of Vascular Surgery, 4*, 80–94.

SANBORN, T. A., CUMBERLAND, D. C., GREENFIELD, A. J., WELSH, C. L. & GUBEN, J. K., 1988. Percutaneous laser thermal angioplasty: initial results and 1 year follow-up in 129 femoro-popliteal lesions. *Radiology, 168*, 121–125.

SMITHSON, P. H., JEANS, W. D. & MURPHY, P., 1989. Installation requirements for an argon laser angioplasty system. *British Journal of Radiology, 62*, 71–73.

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Asymmetrical pulmonary changes in premature infants with surgical closure of a persistent ductus arteriosus

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Abstract. The chest radiographs of 57 premature infants admitted consecutively with hyaline membrane disease and receiving respirator therapy were reviewed, comparing right and left pulmonary abnormalities. Fifteen infants (Group I) did not develop a persistent ductus arteriosus (PDA). Forty-two infants developed a PDA, which was successfully treated with indomethacin in 17 infants (Group II), while in 25 infants (Group III) the ductus was closed surgically. Analysis of the three groups showed that infants who had undergone surgical closure of their PDA developed significantly more asymmetrical broncho-pulmonary damage. Statistically significant fewer radiological findings of broncho-pulmonary damage were found on the left side in comparison with the right side in the group treated surgically.

Premature infants with hyaline membrane disease (HMD) develop lung changes during respirator therapy. Northway et al (1967) described bilateral, rounded, lucent areas alternating with areas of irregular density and chose the term broncho-pulmonary dysplasia (BPD) for this chronic lung syndrome. Swischuk (1977) distinguished between three different types of bubbles found in HMD: in the acute phase of HMD, HMD with pulmonary interstitial emphysema and in the chronic phase of HMD (BPD). We use the term broncho-pulmonary damage pattern introduced by Caffey (1985) because of the overlap of the radiological patterns.

Further reports by Sickles and Gooding (1976), Ablow and Orzalesi (1971), Moylan and Shannon (1979), Tchou et al (1972) and Watts et al (1977) described asymmetrical or localized lung involvement. It has twice been reported that complications such as atelectasis and pneumothoraces can influence the distribution of BPD (Sickles & Gooding, 1976; Watts et al, 1977). The purpose of this study is to investigate the radiological pattern of broncho-pulmonary damage pattern in premature infants with and without surgical closure of their PDA.

Patients and methods

The records of 58 premature infants admitted consecutively to the Neonatal Intensive Care Unit of the University Hospital of Groningen with the diagnosis HMD and needing respirator therapy were reviewed. Of the 58 infants, 15 did not develop a PDA (Group I), while the remaining 43 infants showed this complication. The PDA was diagnosed clinically. In all cases of PDA, closure was attempted primarily with indomethacin, and was successful in 17 cases (Group II). One infant had to be excluded from this group because the ductus was patent post-mortem.

The remaining 25 infants (Group III) underwent surgical closure of their PDA. Gestational age, birth weight, total length of ventilation, peak pressure and peak oxygen concentrations were recorded. Because of the wide range of total length of ventilation, the data were compared after logarithmic transformation. The two groups that developed a PDA were compared with regard to the age at which the ductus was closed. The groups were compared with respect to the clinical data using a one-way analysis of variance. The chest radiographs were then reviewed for asymmetrical distribution of pulmonary abnormalities, and analysed using Fisher's exact test.

Results

Clinical data

Table I gives the mean values of the clinical data of the three groups. The mean values were 28.8 weeks for gestational age, 1191.7 g for birth weight and 21 days for the total length of ventilation, with peak pressures of 28.8 cm of water and peak oxygen concentrations of 86.6%. There were no statistically significant differences between the three groups with regard to birth weight, ventilation pressure, or oxygen concentrations. Infants in Groups II and III were younger than those in Group I (28.8 and 28.1 weeks against 30 weeks, respectively), and Group III was ventilated for a longer period of time (28.6 days against 15.8 and 15 days in Groups I and II, respectively).

There was no significant difference between Groups II and III with regard to the age at which the ductus was closed, even though, in all cases, closure with indomethacin was attempted primarily. Evaluation of the radiographs was later in the two groups that had developed a PDA (Group II, 45.5 days; Group III, 44.5 days) than in Group I (30.4 days). At the time of evaluation, eight (53%) of the 15 infants in Group I were still alive as were 15 (88%) of the 17 infants in Group II and 17 (68%) of the 25 infants of Group III.

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Table I. Composition of study groups

	Group I no PDA	Group II PDA closed with indomethacin	Group III PDA closed surgically	*p* value
Number of infants	15	17	25	—
Gestational age (weeks)	30 ± 2.1	28.8 ± 1.6	28.1 ± 2.2	<0.05
Birth weight (g)	1254.7 ± 356.7	1220 ± 255.4	1134.6 ± 285.2	>0.01
Total length of mechanical ventilation (days)[a]	15.8 ± 12.5	15 ± 11.5	28 ± 21	<0.01
Maximum ventilation pressure (cm water)	29 ± 8.1	27.5 ± 4.4	28.5 ± 5.5	>0.05
Peak oxygen concentration (%)	92 ± 14.2	86.8 ± 18.4	83.2 ± 17.3	>0.05
Age at closure of PDA (days)	—	20.8 ± 14.6	19.7 ± 13.4	>0.05
Day of scoring of radiographs	30.4 ± 1.8	45.5 ± 13.7	44.5 ± 17.6	<0.05
Survivors (%)	8/15 (53)	15/17 (88)	17/25 (68)	

[a] After logarithmic transformation.

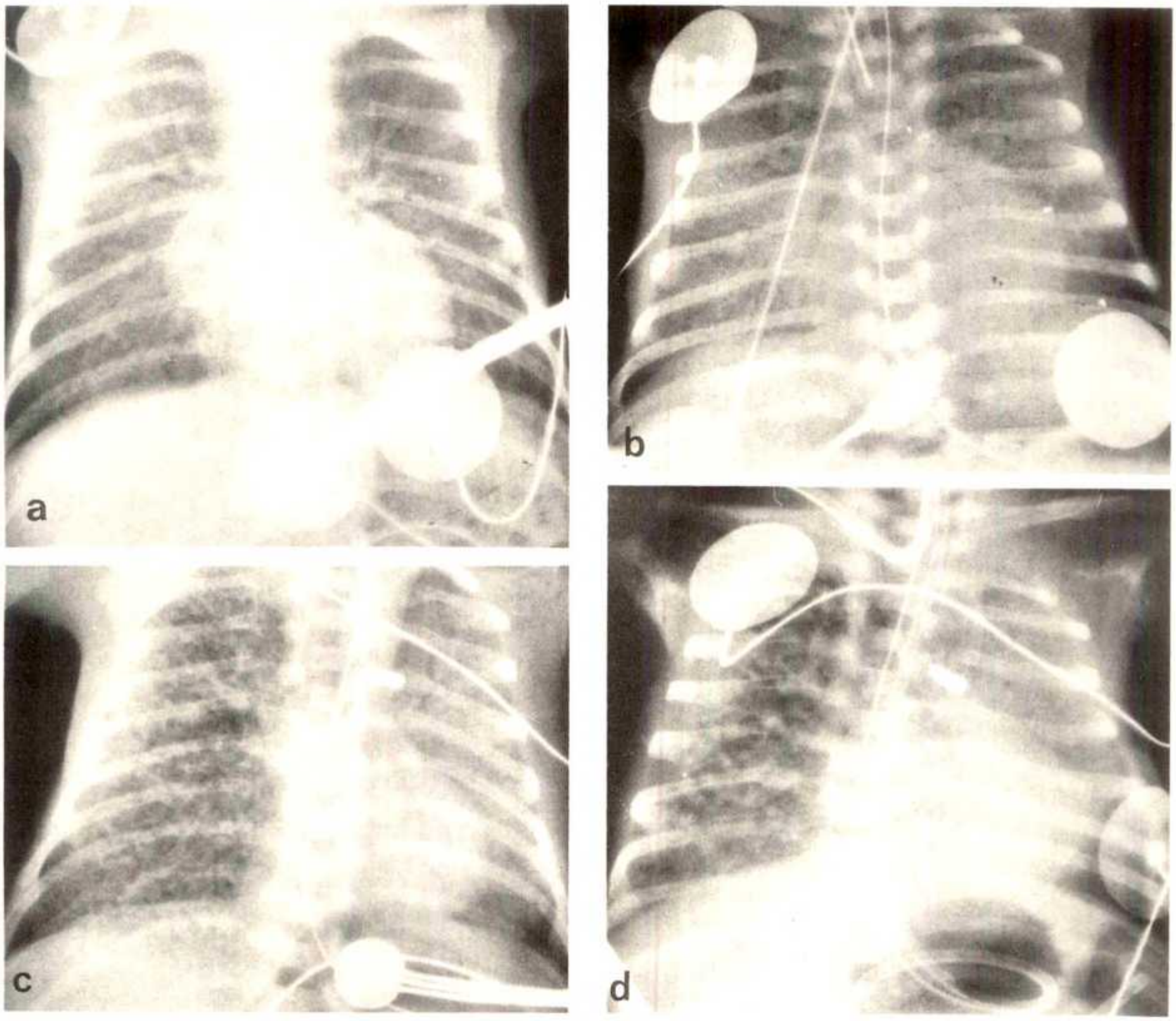

Figure 1. (a) At 3 days post-partum, the chest radiograph of this premature infant shows a symmetrical distribution of the generalized granular pattern of HMD. (b) Two days later, the lungs have become uniformly grey with indistinct heart borders due to the development of a PDA. (c) At 10 days of age and 4 days after the surgical closure of the PDA, the broncho-pulmonary damage pattern is more severe in the right lung, with some interstitial emphysema. (d) On the 15th post-operative day, the difference between the right and the left lung has become more marked.

Table II. Incidence and side of all pneumothoraces

	Group		
	I	II	III
R	7	6	2
L	6	3	27[a]

[a]One infant also had a left-sided pneumothorax pre-operatively.
A bilateral pneumothorax occurred four times in Group I, twice in Group II and once in Group III.

Radiological data

In total, 51 pneumothoraces were diagnosed. In seven cases the pneumothorax was bilateral. In Groups I and II, 13 of the 22 cases of a pneumothorax occurred on the right side with two cases on the right side in Group III. Group III showed 27 left-sided pneumothoraces, Group II three and Group I six. Table II shows the incidence and side of pneumothoraces.

On average the pneumothoraces persisted for 72 h. One infant in Group I was excluded from this analysis because of multiple pneumothoraces on both sides for 8.5 days. Table III gives the results of the scoring of the roentgenograms. Of the 57 infants, 12 showed asymmetrical distribution of their pulmonary abnormalities, while 45 infants showed an equal distribution. In only one infant was the left lung affected more seriously than the right. This child belonged to Group I. Originally, one child in Group II had developed a similar distribution, but was excluded from analysis because the ductus proved to be patent post-mortem. In 11 infants, the right lung was affected more than the left. This type of distribution was seen in nine cases in Group III with one case each in Groups I and II, respectively. There was a significant difference between Groups I and III ($p = 0.04$) and between Groups II and III ($p = 0.026$). Figure 1 shows the chest radiographs of a premature infant with HMD who developed a PDA that was closed surgically and post-operative pulmonary abnormalities that were more severe in the right lung.

Discussion

Although Northway et al (1967) described BPD as a generalized lung disease, Ablow and Orzalesi (1971) and later reports described asymmetrical and localized distributions. Tchou et al (1972) reported 18 infants with asymmetrical lung abnormalities in which the right lung was more severely affected than the left, but dismissed all cases with pneumothorax or atelectasis from the study. Sickles and Gooding (1976) showed that periods of pneumothorax or atelectasis protect that part of the lung from further BPD damage. In their group, unilateral atelectasis or pneumothorax lasted for 4 to 22 days (mean 9.8 days) whilst in our population the pneumothoraces persisted on average for only 3 days. Even though the pneumothoraces lasted for a relatively short time, a protective effect on the left lung was noted despite handling of the left lung during the operative closure of the PDA. Unfortunately, Sickles and Gooding do not give the gestational age of the infants, so comparison of prematurity is difficult. The infants in our study group were smaller than the infants in their population (1191.7 g against 1451.8 g), and presumably were more premature and thus more vulnerable, with faster destruction of the lung fully ventilated. Watts et al (1977) postulate that pneumothoraces reduce the risk of BPD. Based on the same concept, later reports described selective bronchial obstruction ipsilaterally (Mathew & Thach, 1980) and selective bronchial intubation contralaterally in the management of interstitial emphysema in BPD (Vahey et al, 1983).

Table III. Scoring of radiographs

Distribution of pulmonary damage pattern	Group			
	I	II	III	Total
R = L	13	16	16	45
L > R	1	—	—	1
R > L	1	1	9	11
Total	15	17	25	57

Our results suggest that ligation of a PDA, resulting in pneumothorax on the left side, leads to an asymmetrical distribution of the broncho-pulmonary damage pattern in which the right lung is more seriously affected. No literature is available on this specific matter. Radiologists should be aware that a significant group of premature infants with surgical closure of their PDA develop an asymmetrical broncho-pulmonary damage pattern.

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References

Ablow, R. C. & Orzalesi, M. M., 1971. Localized roentgenographic pattern of hyaline membrane disease. *American Journal of Roentgenology*, *112*, 23–27.

Caffey, J., 1985. Idiopathic respiratory distress syndrome. In *Pediatric X-ray Diagnosis*, 8th edn, ed. by F. N. Silvermann (Chicago), pp. 1771–1772.

Mathew, O. P. & Thach, B. T., 1980. Selective bronchial obstruction for treatment of bullous interstitial emphysema. *Journal of Pediatrics*, *96*, 475–477.

Moylan, F. M. B. & Shannon, D. C. 1979. Preferential distribution of lobar emphysema and atelectases in bronchopulmonary dysplasia. *Pediatrics*, *63*, 130–134.

Northway, W. H., Rosan, R. C. & Porter, D. Y., 1967. Pulmonary disease following respirator therapy of hyaline-membrane disease. *New England Journal of Medicine*, *276*, 357–368.

Sickles, E. A. & Gooding, C. A., 1976. Asymmetric lung involvement in bronchopulmonary dysplasia. *Radiology*, *118*, 379–383.

SWISCHUK, L. E., 1977. Bubbles in hyaline membrane disease. *Radiology, 122,* 417–426.

TCHOU, CH.-SH., FLETCHER, B. D., FRANKE, P., OUTERBRIDGE, E. W. & DUNBAR, J. S., 1972. Asymmetric distribution of roentgen pattern in hyaline membrane disease. *Journal of the Canadian Association of Radiologists, 23,* 85–90.

VAHEY, T. N., PRATT, G. B. & BAUM, R. S., 1983. Treatment of localized pulmonary interstitial emphysema with selective bronchial intubation. *American Journal of Roentgenology, 140,* 1107–1109.

WATTS, J. L., ARIAGNO, R. L. & BRADY, J. P., 1977. Chronic pulmonary disease in neonates after artificial ventilation and pulmonary interstitial emphysema. *Pediatrics, 60,* 273–281.

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Ultrasound examination of lymph nodes in the hepato-duodenal ligament

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Abstract. Ninety patients, found to have lymph nodes in the hepato-duodenal ligament (HDL) on ultrasound examination were reviewed over a one-year period in order to define the diseases in which such nodes can be found. The patients were divided into four main groups: benign liver disease ($n = 31$), malignant disease ($n = 26$), disease of the gallbladder or the biliary tree ($n = 14$) and a group with various benign, most inflammatory diseases ($n = 19$). In 40% of the patients (36/90), the lymph nodes in the HDL were the only sign of disease on ultrasound examination, and the majority of those were in the benign group.

Patients with abnormal liver function tests or upper abdominal pain are often examined initially with ultrasound. A changed echo pattern of the liver with fatty infiltration can usually be detected (Taylor et al, 1976; Foster et al, 1980), whereas to diagnose mild cirrhosis without fatty infiltration and chronic active hepatitis and related diseases is often difficult or impossible (Dewbury & Clark, 1979). The finding of abnormal lymph nodes in the hepato-duodenal ligament (HDL) might, however, indicate the presence of liver disease and detection of nodes in the HDL by ultrasound is feasible (Forsberg & Hederström, 1985; Forsberg et al, 1987).

The nodes surrounding the hepatic artery ventral to the portal vein are generally those observed, but nodes can also be seen dorsal to the portal vein. Nodes in the HDL in chronic active hepatitis have been reported on computed tomography (CT) (Gore et al, 1988). Lymph nodes in the HDL can be seen in patients with benign as well as malignant diseases (Baker et al, 1987; Hederström & Forsberg, 1987): in anatomical atlases they are called hepatic nodes and drain mainly the hepato-biliary system. In this study, however, lymph nodes were noted in patients with diseases of other organs as well, indicating lymph drainage to the nodes in the HDL, directly or indirectly. The aim of this review was to define those diseases in which nodes in the HDL can be detected by ultrasound.

Material and methods

The study covered 90 consecutive patients, 63 female and 27 male, with a mean age of 56 years (range 4–91 years), examined over a one-year period, in whom nodes (>0.5 cm) were observed in the HDL on ultrasound examination. All patients were examined with dynamic ultrasound using 3.5 MHz and 5 MHz mechanic sector scan transducers and all the examinations were performed by radiologists with extensive experience in ultrasound. Most patients had been fasting for 4 to 12 h before the examination. The echogenicity and the homogeneity of the liver parenchyma and the size and echogenicity of the lymph nodes in the HDL were registered. The nodes were sometimes flattened or oval in shape, in which case the largest measurements were noted. Measured in retrospect, the nodes were subdivided into four groups according to size (Table I).

Follow-up of 6 months (deceased patients) to 3 years later was made by studying case records. Histopathological diagnosis was available from autopsy in six cases, and from biopsy or surgery in 50 cases. In the remaining 34 cases the final diagnosis was obtained from clinical findings, including liver function tests (serum bilirubin, alkaline phosphatase, aminotransferase and γ-glutamyltransferase) and radiological examinations.

The patients were divided into four main groups depending on diagnosis: benign liver disease ($n = 31$), malignant disease ($n = 26$), disease of the gallbladder or the biliary tree ($n = 14$) and a group of miscellaneous diseases ($n = 19$). A patient who had a gallstone or had had a cholecystectomy was classified as having gallbladder disease, since we noted that the nodes in the HDL seen in patients with cholecystitis do not seem to disappear after cholecystectomy.

Malignant disease overrode the diagnosis of benign disease.

Results

Benign liver disease

This was found in 31 patients (Table II). A histological diagnosis was available for 25 of these and the final diagnosis was established from clinical findings in six cases.

Table I. Lymph nodes in the hepato-duodenal ligament

Size of node (cm)	Group	Size of node (cm)
	I	<1.0
1.0	≤II	<1.5
1.5	≤III	<2.0
2.0	≤IV	

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Table II. Benign liver disease (31 patients)

	Number of patients	Ultrasound of the liver		Liver tests		Lymph nodes			
		Normal	Abnormal	Normal	Abnormal	I	II	III	IV
Hepatitis	13	7	6		13		4	1	8
Hepatopathy	5	4	1		5		2	1	2
Cirrhosis	11	6	5		11	1	3	4	3
Drug side-effect	2	1	1		2	1	1		
Total	31	18	13		31	2	10	6	13

All the patients had abnormal liver function tests, and in most cases the levels were seriously abnormal.

Thirteen patients had an abnormal echo pattern of the liver parenchyma: grossly irregular liver structure in six cases, increased echogenicity of the parenchyma in four cases (as is often seen with fatty infiltration) and decreased echogenicity in three cases.

Among the 13 patients with hepatitis, eight had nodes $\geqslant 2.0$ cm. The other three subgroups showed irregularity in size of the nodes.

Malignant disease

This was found in 26 patients, with a histological diagnosis available for 24 cases. The final diagnosis was made from a radiological examination in two cases (Table III).

Twenty patients had abnormal liver function tests, four were normal and in two cases no tests were available.

In three patients the liver parenchyma could not be evaluated because of bowel gas in two patients and dilated biliary ducts in one patient. An abnormal echo pattern of the liver was found in 15 patients: the liver structure was irregular owing to malignant infiltration in 12 cases and non-malignant causes in one case; the echogenicity was increased in one case and decreased in one case.

Eight patients had a normal echo pattern of the liver: the ultrasound examination showed a tumour of the pancreas in one of these patients; a patient with chronic lymphocytic leukemia had a considerably enlarged spleen and two patients with ovarian tumours had ascites.

All patients except one had lymph nodes that were 1.0 cm or larger. Of these, half ($n = 13$) had nodes of at least 2.0 cm, and the other half ($n = 12$) had nodes between 1.0 cm and 2.0 cm.

Disease of the gallbladder or the biliary tree

Such disease was found in 14 patients (Table IV), histologically confirmed in eight cases. Final diagnosis was made from clinical findings in six cases.

One patient with previous cholecystectomy had normal liver function tests, and the remaining 13 patients had abnormal tests. Abnormal echogenicity of the liver was observed in five patients; irregular liver structure in two cases; increased echogenicity in two cases and decreased echogenicity in one case.

Ultrasound showed normal liver parenchyma in nine patients: five of these had gallstones or dilated bile ducts.

The size of the nodes in the different subgroups was irregularly distributed.

Table III. Malignant disease (26 patients)

	Number of patients	Ultrasound of the liver			Liver tests			Lymph nodes			
		Normal	No results available	Abnormal	Normal	No results available	Abnormal	I	II	III	IV
Liver metastases	13		1	12			13		4	2	7
Carcinoma of the gastro-intestinal tract and pancreatic carcinoma, without liver metastases	6	3	1	2	2	1	3		3	1	2
Lymphatic malignancy	3	2		1	1		2		1		2
Ovarian tumour	2	2			1	1			1		1
Hypernephroma	1		1				1				1
Carcinoma of the lung	1	1					1	1			
Total	26	8	3	15	4	2	20	1	9	3	13

Table IV. Disease of the gallbladder or biliary tree (14 patients)

	Number of patients	Ultrasound of the liver		Liver tests		Lymph nodes			
		Normal	Abnormal	Normal	Abnormal	I	II	III	IV
Cholangitis/cholecystitis	6	4	2		6		1	3	2
Cholecysto-/docholithiasis	6	4	2		6	1	2	2	1
Previous cholecystectomy	2	1	1	1	1		1	1	
Total	14	9	5	1	13	1	4	6	3

Benign, mostly inflammatory diseases

These were found in 19 patients (Table V), confirmed histologically in four cases and by clinical examination in 15 cases.

Liver function tests were normal in eight patients and abnormal in 11. An abnormal echo pattern of the liver was found in four cases: irregular in one patient, increased echogenicity in one and decreased echogenicity in two patients.

For the majority of patients ($n = 15$), ultrasound examination showed normal liver parenchyma; five of these had pancreatitis. Even in this group of miscellaneous diseases, the size of the lymph nodes varied considerably.

Discussion

In the abdomen, the term "ligament" refers to a fold of peritoneum supporting any of the abdominal viscera. A peritoneal ligament consists of two layers of peritoneal membrane and the mesodermal tissue, blood vessels and lymphatic structures enclosed between the two layers. The stomach is entirely covered with peritoneum. A double layer of peritoneum, the lesser omentum, includes the hepato-gastric ligament extending from the ligamentum venosum of the liver to the lesser curvature of the stomach, and the HDL passing from the porta hepatis to the pyloric region and the upper horizontal portion of the duodenum. The free edge of the HDL, through which run the portal vein, the hepatic artery, the common bile duct and the hepatic lymph vessels, forms the ventral margin of the epiploic foramen (foramen of Winslow), which gives access to the lesser peritoneal sac (bursa omentalis) (Netter, 1979; Balfe et al, 1984; Weill et al, 1986).

The lower third of the oesophagus, the gastric wall, the duodenum, the small intestine and the proximal portion of the large intestine drain partly into the coeliac (middle supra-pancreatic) nodes, which are situated above the pancreas and around the coeliac artery and its branches. The pancreas also drains into the coeliac nodes and to the chain of hepatic nodes along the bile ducts. The lymph from the liver, the gallbladder and from most of the extrahepatic bile ducts drain into the hepatic lymph nodes around the common bile duct and the main stem of the portal vein. The lymphatic vessels continue to the chain of coeliac nodes (Netter, 1979).

Since the vast majority of patients do not routinely show any lymph nodes in the HDL (Fig. 1), one can assume that normal hepatic nodes cannot be visualized by ultrasound. One explanation might be that they are both small (<0.5 cm) and have an echogenicity of about the same level as the surrounding fat. Nodes associated with inflammatory or malignant disease become enlarged or display decreased echogenicity. Lymph nodes, even of small size, with an echopoor appearance might indicate disease.

Abnormal lymph nodes in the HDL are usually rounded or oval and can often be distinguished from each other by the fat and connective tissue preserved between the nodes. When echopoor lymph node aggregations are present in the HDL, the hepatic artery

Table V. Miscellaneous diseases (19 patients)

	Number of patients	Ultrasound of the liver		Liver tests		Lymph nodes			
		Normal	Abnormal	Normal	Abnormal	I	II	III	IV
Gastritis/duodenitis/peptic ulcer	6	6		3	3		3	2	1
Pancreatitis	6	5	1	2	4	1	4	1	
Colitis	3	2	1	1	2			1	2
Salmonella paratyphi sepsis	2		2	1	1	1			1
Amoebic dysentery	1	1		1					1
Collagen disease	1	1			1			1	
Total	19	15	4	8	11	2	7	5	5

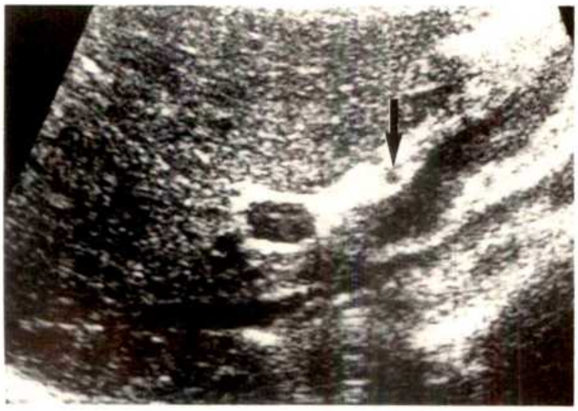


Figure 1. Longitudinal scan through normal hepato-duodenal ligament. The hepatic artery (arrow) is surrounded by fat.

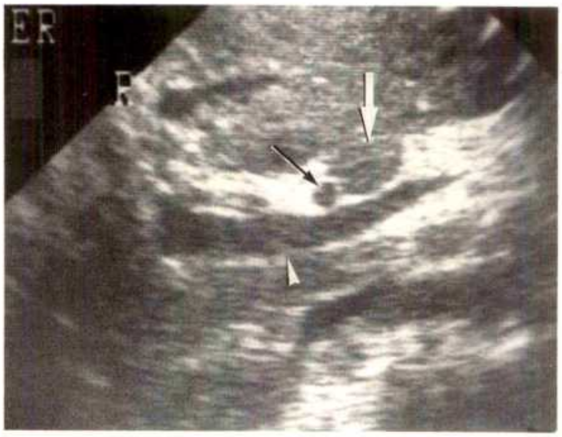
acquires a very bright delineation creating the appearance of a halo around the artery when scanned transversely (Fig. 2).

The proximity to the duodenal bulb, together with obscuring gas, sometimes make the ultrasonic visualization difficult. Examining the patient in a sitting position may be helpful. The skill and experience of the ultrasonographer is of decisive importance for the detection of lymph nodes in the HDL.

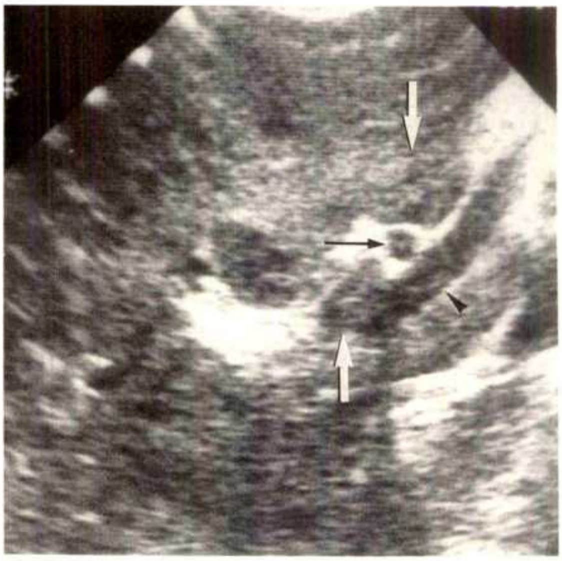
The absolute size of the lymph node seems to be of minor importance in most cases. We noted a considerable variation in the size of the lymph nodes in the various groups of diseases. In the malignant group, 50% (13/26) of the lymph nodes were less than 2 cm, and this was also the case in 67% (43/64) of the nodes in the benign group. This is in agreement with the review of abdominal lymphadenopathy in benign disease detected by CT by Deutch et al (1987) who found that the size of lymph nodes is not useful to differentiate benign from malignant processes. Patients react differently with regard to the degree of node enlargement and change in node echogenicity, independent of the underlying disease. Not every patient with acute hepatitis, for instance, has enlarged lymph nodes in the HDL. If nodes are present, their size shows a substantial variation from one patient to another. Possibly there is a change in the size of lymph nodes during the course of a disease (Gore et al, 1988).

Extensive abdominal lymphadenopathy is most often caused by lymphoma and metastatic disease, but can also be observed in a number of benign entities. Lymph nodes respond to a variety of external stimuli, including inflammatory, infectious, systemic and immunologic disorders, as well as malignant processes (Deutch et al, 1987).

The lymph nodes of the HDL, especially those situated close to the hepatic artery, seem to be involved not only in diseases of the biliary tract and in widespread malignant disease but also directly or indirectly in inflammatory diseases of the gastro-intestinal tract. This finding is supported well by our knowledge of the complex lymphatic system in this region.



(a)



(b)

Figure 2. Oblique scan along portal vein–splenic vein (arrowhead). Irregular liverparenchyma owing to metastases. (a) A "halo" around the hepatic artery (small arrow) and an enlarged lymph node (large arrow) caudal to the artery and dorsal to the liver. (b) The hepatic artery (small arrow) is surrounded by two large lymph nodes (large arrows).

In this study about one third of the patients (26/90) had malignant disease causing lymph node enlargement in the HDL, whereas Deutch et al (1987) found malignant disease causing abdominal lymph node enlargement in 94% of the patients on CT. Our material, however, consists only of patients with lymph nodes in the HDL, whereas Deutch's material included abdominal lymphadenopathy in general. As described by Baker et al (1987), the HDL is difficult to evaluate using axial CT because of its oblique orientation, anatomic variability, paucity of fat and compact volume. Since ultrasound has the advantage of unlimited scan planes, it may show a small periportal abnormality with more certainty than CT, especially in a patient with a thin body habitus.

More than half of the patients with benign liver disease (18/31) had lymph nodes in the HDL as the only sign of disease on ultrasound examination. This compares favourably with previous work by Forsberg et al (1987, 1985), who have shown that ultrasonic visualization of lymph nodes in the HDL seems to increase the possibility of detecting early diffuse liver disease even when the liver parenchyma appears sonographically normal.

Only a few (4/26) patients in the malignant group presented with lymph nodes in the HDL as the only sign of disease on ultrasound scans, while half of those in the benign group did so (32/64).

It is well known that malignancies which metastasize by means of the lymphatics cause enlargement of regional as well as distant lymph nodes. In the malignant group in our material, the tumour was located in the abdomen in 22 of the 26 cases.

Most of the patients in the biliary group (10/14) presented with other signs of disease, such as abnormal echogenicity of the liver parenchyma, gallstones or dilated biliary ducts which are sonographically easily detectable, and it is reasonable to assume, because of the anatomy, that disease of the gallbladder and the biliary tree, as well as benign liver disease, may cause changes in echogenicity and size of the lymph nodes in the HDL (Forsberg & Hederström, 1985; Deutch et al, 1987; Forsberg et al, 1987; Hederström & Forsberg, 1987; Gore et al, 1988).

About a quarter (19/90) of the patients in our study had a disease that was neither malignant nor located in the hepato-biliary tract. Twelve patients had inflammatory or infectious disease of the gastro-intestinal tract; the pancreas was involved in six cases and there was one case of collagenosis. Half of the patients (10/19) in the miscellaneous group had no other sign of disease than the lymph nodes in the HDL, which accords with the limited ability to detect inflammatory gastro-intestinal disease with ultrasound. A possible, indirect way that the lymph nodes in the HDL may be affected is by the blood flow from the gastro-intestinal tract through the portal vein to the liver, since the lymphatics from the liver drain into the lymph nodes in the HDL. In this way, lymph nodes in the HDL might indicate bowel disease.

In 50 patients with normal liver parenchyma on ultrasound examination, the lymph nodes in the HDL indicated disease in the upper abdomen. Of these, there were four patients in the group of malignant diseases, five patients in the biliary group and five patients in the group of miscellaneous diseases with other pathological findings on ultrasound examination. Thus in 40% of the patients (36/90), the nodes in the HDL were the only sonographic sign of disease.

Sometimes lymph nodes in the HDL are the only finding observed on ultrasound examination in a patient with abdominal pain, indicating that further investigation and follow-up should be considered. Nodes in the HDL might indicate inflammatory disease of the abdomen, and could be a parameter with which to follow the course of disease during treatment. Further studies of this group of patients without malignancy or hepato-biliary disease are warranted.

References

BAKER, M. E., SILVERMAN, P. M., HALVORSEN, R. A. & COHAN, R. H., 1987. Computed tomography of masses in periportal/hepatoduodenal ligament. *Journal of Computer Assisted Tomography, 11*, 258–263.

BALFE, D. M., MAURO, M. A., KOEHLER, R. E., LEE, J. K. T., WEYMAN, P. J., PICUS, D. & PETERSON, R. R., 1984. Gastrohepatic ligament: normal and pathologic CT anatomy. *Radiology, 150*, 485–490.

DEUTCH, S. J., SANDLER, M. A. & ALPERN, M. B., 1987. Abdominal lymphadenopathy in benign diseases: CT detection. *Radiology, 163*, 335–338.

DEWBURY, K. C. & CLARK, B., 1979. The accuracy of ultrasound in the detection of cirrhosis of the liver. *British Journal of Radiology, 52*, 945–948.

FORSBERG, L., FLORÉN, C. H., HEDERSTRÖM, E. & PRYTZ, H., 1987. Ultrasound examination in diffuse liver disease. Clinical significance of enlarged lymph nodes in the hepatoduodenal ligament. *Acta Radiologica, 28*, 281–284.

FORSBERG, L. & HEDERSTRÖM, E., 1985. The lymph nodes of the hepatoduodenal ligament in non-malignant hepatobiliary disease. *Journal of Ultrasound in Medicine and Biology, Supplement No. 1*, p. 86.

FOSTER, K. J., DEWBURY, K. C., GRIFFITH, A. H. & WRIGHT, K., 1980. The accuracy of ultrasound in the detection of fatty infiltration of the liver. *British Journal of Radiology, 53*, 440–442.

GORE, R. M., VOGELZANG, R. L. & NEMCEK, A., 1988. Lymphadenopathy in chronic active hepatitis: CT observations. *American Journal of Roentgenology, 151*, 75–78.

HEDERSTRÖM, E. & FORSBERG, L., 1987. Ultrasonography in carcinoma of the gallbladder. *Acta Radiologica, 28*, 715–718.

NETTER, F. H., 1979. *The CIBA collection of medical illustrations, Vol. 3, Digestive system, Parts I–III*, (CIBA Pharmaceutical Company, London).

TAYLOR, K. J. W., CARPENTER, D. A., HILL, C. R. & MCCREADY, V. R., 1976. Gray scale ultrasound imaging. The anatomy and pathology of the liver. *Radiology, 119*, 415–423.

WEILL, F., WATRIN, J., ROHMER, P., WEILER, S. & COCHE, G., 1986. Ultrasound and CT of peritoneal recesses and ligaments: a pictorial essay. *Ultrasound in Medicine & Biology, Vol. 12, No. 12*, 977–989.

1990, *The British Journal of Radiology*, *63*, 31–32

Calcification of the intrathoracic trachea demonstrated by computed tomography

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Abstract. The presence of intrathoracic tracheal calcification was assessed on computed tomographic (CT) scans of 90 consecutive male and female patients. The presence of calcification was demonstrated to be common and to increase with age. No female preponderance was shown.

Tracheal calcification observed on plain chest radiographs is said to be a result of aging and is more common in females (Fraser & Paré, 1977). The greater contrast sensitivity of computed tomography (CT) would be expected to show a higher prevalence of tracheal calcification. The aims of this retrospective study were to confirm the effects of age and to compare the prevalence in men and women.

Patients and methods

The CT examinations of 90 male and 90 female patients obtained retrospectively from consecutive investigations of the thorax were reviewed. Patients with known or suspected tracheal disease and those in whom the whole length of the intrathoracic trachea was not examined were excluded. Indications included a wide range of mediastinal, pulmonary and chest wall lesions, and all examinations were performed on an IGE 9800 scanner with the patient supine and during suspended maximum inspiration. Contiguous sections 1 cm thick were obtained and the data processed using a standard algorithm with display on a 512 × 512 matrix. The presence of calcification was assessed in the intrathoracic trachea from hard copies recorded at appropriate window settings by two independent observers (D.C.L. and P.M.T.). Where there was a difference of opinion between the two observers, the radiographs were reviewed jointly and agreement reached.

Results

The presence of calcification is shown in Table I. With increasing age there was an increasing proportion of patients with tracheal calcification, and above 60 years slightly more men were affected.

Discussion

Calcification can occur in the cartilaginous rings or the mucosa of the trachea. Physiological calcification is confined to the cartilaginous rings. It is commonly seen

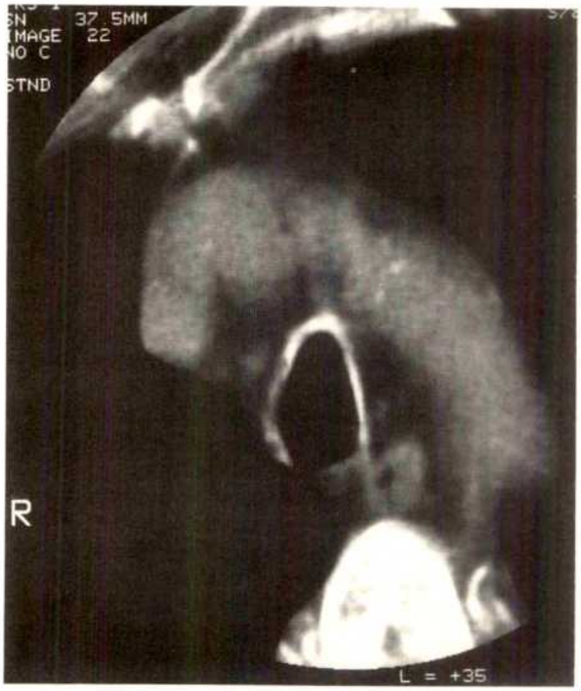

Figure 1. Computed tomographic section in a 64-year-old man showing marked tracheal calcification.

Table I. The prevalence of observed calcification

	Age (years)	Calcification present	Total number in group	Percentage with calcification
Male	20–39	0	12	0
	40–59	8	31	25.8
	60–79	31	47	65.2
Female	20–39	0	20	0
	40–59	9	33	27.2
	60–79	15	37	40.5

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on conventional chest radiography, usually in the elderly, and is said to be more frequent in females (Fraser & Paré, 1977). Cartilaginous calcification is rarely seen congenitally (Mlynarski et al, 1985) and has been noted following cardiac surgery in children (Rifkin & Pritzker, 1984). It also occurs in patients with hypercalcaemia and hyperphosphataemia. The lesions seen in tracheopathia-osteoplastica are thought to arise from abnormal cartilaginous foci occurring within the mucosa. The CT appearances of these lesions have been previously described (Onitshuki et al, 1983; Hirsch et al, 1985).

Interrogation of the images provided little additional information: the presence of calcification was usually evident on the hard-copy images. Moreover, small areas of calcification could possess erroneously low attenuation values due to partial volume averaging. The presence of calcification should be distinguished from "streak" artefact occurring at interfaces, particularly where there is associated motion. "Streak" is common but is characterized by extension beyond the tracheal wall, a linear configuration and being more commonly seen in those portions of the tracheal wall adjacent to vessels. Measurement of attenuation values again proved to be unhelpful as erroneously high values were produced by "streak".

The high incidence of tracheal calcification demonstrated may be expected because of the greater contrast resolution of CT compared with conventional radiography. We have confirmed the relationship with age and demonstrated no female preponderance. In the older age group the prevalence appears slightly greater in males, although this may be because of the higher mean age of men in this group (male = 69.1 years, female = 65.4 years).

In conclusion it should be realized that tracheal calcification is a common finding and may be encountered in relatively young patients.

References

Fraser, R. G. & Paré, J. A. P. (Eds), 1977. *The Diagnosis of Diseases of the Chest*, second edn (W. B. Saunders, Philadelphia), p. 476.

Hirsch, M., Goldstein, J., Tovi, F. & Gerzof, S. G., 1985. Diagnosis of tracheopathia osteoplastica by computed tomography. *Annals of Otology Rhinology and Laryngology*, *94*, 217–219.

Mlynarski, F. G., Parnes, S. M. & Polanski, S., 1985. Congenital calcification of the larynx and trachea. *Otolaryngology—Head and Neck Surgery*, *93*, 99–101.

Onitsuki, M., Hirose, N., Watanabe, K., Nishitani, H., Kawahira, K., Matsuura, K. & Shigematsu, N., 1983. Computed tomography of tracheopathica osteoplastica. *American Journal of Roentgenology*, *140*, 268–270.

Rifkin, M. D. & Pritzker, H. A., 1984. Tracheobronchial cartilage calcification in children. Case reports and review of the literature. *British Journal of Radiology*, *57*, 293–296.

1990, *The British Journal of Radiology*, *63*, 33–40

Assessment and comparison of chest radiography techniques in the United States and Sweden

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Abstract. The United States Center for Devices and Radiological Health and the Swedish National Institute of Radiation Protection started a collaborative project in 1983. The purpose of the project was to test the adequacy and practicability of the United States (US) Nationwide Evaluation of X-ray Trends (NEXT) programme in Sweden. The NEXT protocol for the postero-anterior chest projection was modified and expanded to make it both "statistical" and "investigational" (in the US, NEXT gives mainly "statistical" information). All chest X-ray units in Sweden were surveyed in 1986–87. The project showed that the NEXT programme is applicable to countries other than the United States and provides a standardized protocol that enables intercomparison of the radiological techniques. This paper presents the comparison of the radiological techniques used in Sweden and the United States. The results of the investigational modifications made to the protocol used in Sweden are discussed. Recommendations concerning expansion of the NEXT protocol to include these valuable tools for investigational surveys are presented.

Radiation protection practices in diagnostic radiology have been well established in both Sweden and the United States (US) for many years, although the approaches vary between the two countries. In Sweden, the National Institute of Radiation Protection (NIRP) has more direct impact on the user of diagnostic X-ray equipment than does the Center for Devices and Radiological Health (CDRH) in the United States. In the United States, State Radiation Control personnel deal directly with individual facilities, perform inspections of equipment in use, and, through their regulations, attempt to ensure that both equipment and practices in facilities are appropriate. The CDRH deals with manufacturers in a regulatory sense only to ensure that equipment when first manufactured and installed meets appropriate standards. They also issue recommendations on appropriate use of equipment and technique. In Sweden, the NIRP performs all the above functions.

There is considerable variation in the resources available to the various states in the United States to conduct their radiation protection programmes in diagnostic radiology. Thus, one might suspect that there will be considerably more variation in the effectiveness of these programmes in the United States than one would find in Sweden, where a national organization is responsible for practices throughout the country.

This paper presents the results of a collaboration between the Swedish NIRP and the United States CDRH to examine the methods used in conducting chest radiography in the two countries and to see if these variations, mentioned above, exist in actual practice. Chest radiography was selected because it is the most common X-ray examination performed in each country, and it may also be easier to assess than other examinations because of the relative standardization in the way in which it is conducted.

Health care system in the United States

The health care system in the United States is generally a private, fee-for-service system. There is no overall federal regulation or control of the system, neither in general nor for the use of X-ray equipment in particular.

In the case of X-ray diagnosis, the equipment performance at the time of installation is covered by a Federal performance standard. The standard is enforced in local facilities by spot checks performed by State Radiation Control personnel. Considerable guidance exists on a great many aspects of proper radiation protection; *e.g.* conduct of examinations, quality assurance and patient selection. This voluntary guidance is developed by such international and national groups as the International Commission on Radiation Protection (ICRP), the National Council on Radiation Protection (NCRP), the American Association of Physicists in Medicine (AAPM), the American College of Radiology (ACR) and the CDRH.

The Swedish health care system

The most striking difference between the health care systems in the United States and Sweden is that, by tradition, most health care in Sweden is provided by the public health care system. Ninety-five per cent of all X-ray examinations are done at facilities belonging to the public health care system.

Radiation protection in medicine has a long tradition in Sweden. As early as the 1920s, countrywide checks and dose measurements were performed at the X-ray therapy facilities. In 1941, the first radiation protection act was issued and inspections from the central authority have been performed since that time, also covering the diagnostic departments. The NIRP, a governmental authority since 1965, has the mandate to issue regulations, carry out inspections and grant licences. In 1983, quality control became mandatory for all medical X-ray diagnostic facilities. Not all health districts have yet managed to meet these demands fully, but much has been done and it seems that in the near future the situation will be quite satisfactory.

With this background, it is interesting to see what differences exist between Swedish and American radiology, and to see if the expectations of more homogeneity in Sweden versus more variety in the United States are reflected in the results of the surveys.

NEXT in the United States

The Nationwide Evaluation of X-ray Trends (NEXT) programme has been in existence in the United States since October 1972, and has been reported previously (Bunge et al, 1979; Butler et al, 1985). This programme, a co-operative effort between state radiological health programmes and the CDRH, aims to provide meaningful radiation exposure and technique data for the participating agencies to use in setting priorities for planning to improve specific areas of radiation protection. The data are also useful for characterizing the practice of radiology during specific time periods and measuring changes with time.

The programme was revised in 1984 to address problems with statistical sampling and to incorporate newer survey techniques. A new survey protocol is designed for each projection to be studied. The first such protocol was for the postero-anterior (PA) chest projection.

Introduction of NEXT in Sweden (the ENCUSS project)

The NEXT programme was designed for American conditions, and it is not self-evident that its adoption by other countries would result in the same benefit. It may be necessary to modify the procedure in order to receive the maximum benefit or the procedure may not be applicable because of differences in equipment and techniques applied.

Thus, the CDRH in the United States and the NIRP in Sweden agreed on a collaborative project called ENCUSS (expanded NEXT collaboration between the United States and Sweden). The aims of this project were as follows.

1. Checking the adequacy and the practicability of the new NEXT programme in Sweden.
2. Introduction of modifications and expansions that might be incorporated into the NEXT programme.
3. Finding a proper design for an "investigational" survey, *i.e.* a survey giving sufficient information so that corrective actions for an individual unit can be taken (whereas NEXT gives mainly "statistical" information).
4. Investigating the similarities and differences between United States and Swedish X-ray diagnostic techniques.
5. Mutual exchange of experience in the field of governmental radiation protection.

The main accomplishments of the project were, briefly, that a pilot study was designed to cover all full-size chest X-ray units in the county of Stockholm, approximately 75 units. The survey contained the current NEXT procedure and additional elements that were agreed on by the two authorities. The basic measuring equipment and the data processing were supplied by the CDRH. After evaluation of the pilot study, a survey covering the whole country was performed.

On the basis of the experience gained in this survey, two procedures have been worked out: one for "statistical" evaluations (*i.e.* the current NEXT procedure with some slight modifications) and one for the identification of necessary corrective actions for the individual units.

In this paper, the results of ENCUSS are presented and, on the basis of the outcome of the surveys performed in the United States and in Sweden, the similarities and differences in chest radiography between the two countries are discussed.

Methods

The current NEXT programme in the United States consists of the development of a survey protocol for a selected examination, establishing a population of facilities nationwide that carry out that examination and drawing a statistically valid sample from that population to be surveyed. Normally, the physical surveys of the facilities are conducted by State Radiation Control personnel. In this way, an estimate of the average exposure to persons undergoing that examination can be developed. Other data relating to the way the examination is conducted are also collected.

In order to survey facilities using automatic exposure control (AEC) X-ray equipment, it is necessary to have available an attenuation phantom to simulate the average patient. A phantom was developed for the chest projection, called the LucAl phantom, which has been described elsewhere (Conway et al, 1984). A procedure was also developed for assessing the performance of automatic processors via the use of a reference film and a calibrated sensitometer (called sensitometric technique for evaluation of processing (STEP), Suleiman et al, 1982).

Data collected during the survey include radiation exposure, workload, beam quality, film density, technique normally used, film processor operation, film-screen combination normally used and type of X-ray equipment used. The survey protocol and equipment used are described in more detail elsewhere (Butler et al, 1985).

Modifications of the NEXT procedure used in the United States were made prior to implementing the programme in Sweden. All elements of the United States survey were retained, but several additional measurements were added to the protocol. These included measuring the air kerma in the imaging plane

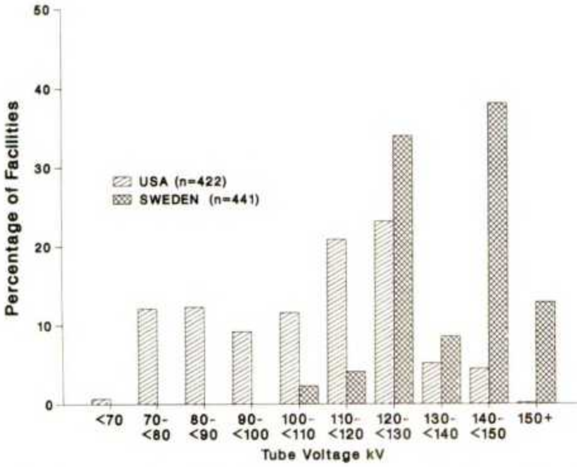

Figure 1. Distributions of tube voltage used for the chest examination in the United States and Sweden.

by means of a reference cassette while recording the air kerma in front of the phantom simultaneously with an ionization chamber. The sensitometry test, *i.e.* the STEP procedure, was extended to the film used at the facility. A radiograph was taken with an image test device attached behind the first absorption layer of the LucAl phantom, containing a lead-bar test pattern and low-contrast objects.

In the United States, a statistical sample of facilities was chosen, whereas the survey in Sweden covers every stationary chest unit used for full-sized radiographs in the country, a total of 441 units.

Results

There was a much wider variety of techniques used in the surveyed United States facilities than was found in Sweden. The tube voltage used in Sweden is in the range of 100–150 kV, while in the United States ~35% of the facilities use a tube voltage <100 kV (Fig. 1). Also, many facilities in Sweden use additional filtration, which in combination with the higher tube voltage results in a higher mean half-value layer (HVL) in Sweden than in the United States. In Sweden, the mean HVL was 6.0 mm Al (range 2.5–13.0 mm Al), whereas in the United States the mean HVL was 4.1 mm Al (range 1.8–9.5 mm Al, Fig. 2).

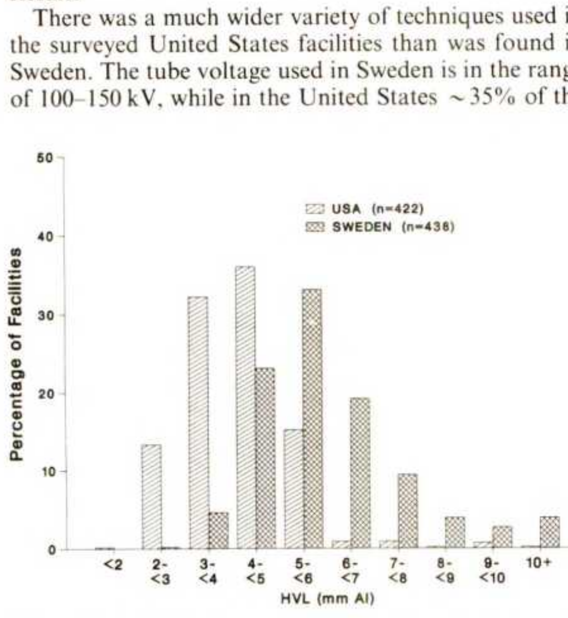

Figure 2. The distribution of first HVL values for chest examinations in the United States and Sweden.

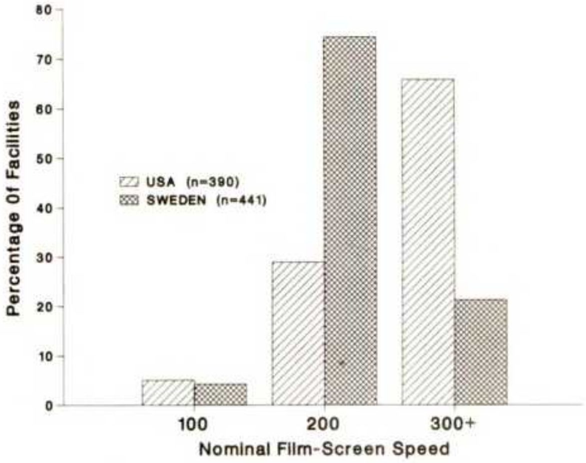

Figure 3. The distribution of nominal speed of film–screen systems used for chest examinations in the United States and Sweden.

All Swedish facilities used some method of scatter suppression, mostly a grid (423 of 441 facilities), with the remaining 18 facilities using an air gap. In the United States, ~25% of the facilities used no scatter suppression. Most of the facilities not using scatter suppression were operating at tube voltages <100 kV.

The percentage of facilities using AEC is somewhat higher in Sweden (65%) than in the United States (54%).

The distribution of the exposure times is virtually the same in the two countries. Twenty-five per cent of the X-ray units in the United States are single-phase units versus none in Sweden. The generally lower inherent output of single-phase compared with multi-pulse equipment must be offset by other parameters, such as filtration and film–screen speed. An exposure time exceeding 40 ms was observed at roughly 10% of the facilities in both countries.

A widely used measure for the speed of film–screen systems is the speed index. It is defined as the reciprocal value of the air kerma measured in milligrays that will produce an optical density of 1.0 above base plus fog on the processed film. Figure 3 shows the speed of the film–screen systems used in the two countries: about two-thirds of the systems used in Sweden have a speed index of 200, whereas in the United States an index of 300 or higher is the most common, indicating the use of generally faster systems in the United States. The nominal speed could not be assigned to all film–screen systems in the United States survey owing to lack of

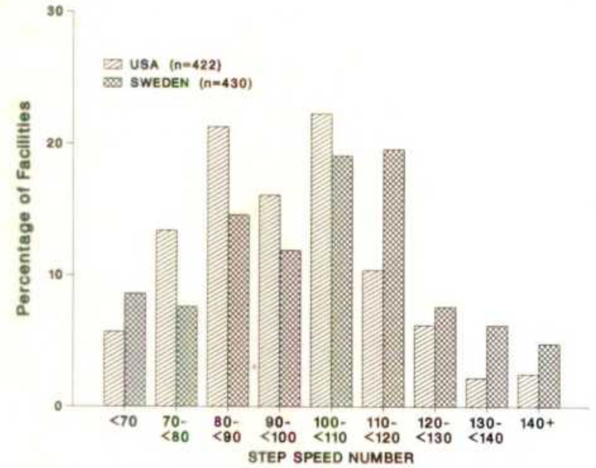

Figure 4. The distribution of STEP speed for automatic film processors in the United States and Sweden.

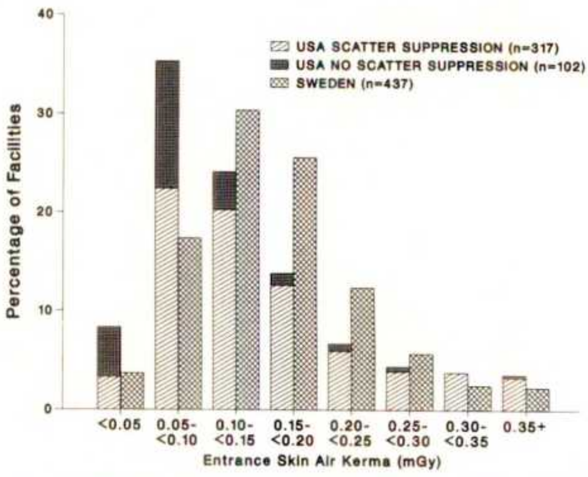

Figure 5. The entrance skin air kerma (ESK) values for the PA chest examination in the United States and Sweden.

information in the literature, from suppliers and from manufactures for some of the film–screen combinations reported.

The STEP evaluation of automatic processing reveals that processing speed is somewhat higher in Sweden than in the United States. On the average, the Swedish facilities tend to overprocess, while the United States facilities tend to underprocess (Fig. 4).

In the NEXT protocol, the assessment of patient dose is based on the entrance skin exposure (ESE), given as the exposure in the entrance skin surface plane without backscatter, measured in milliroentgens (mR) (Bunge et al, 1979). Since the roentgen is abandoned in the SI system, the ESE values are replaced by entrance skin air kerma (ESK) values, *i.e.* the air kerma at skin entrance without backscatter.

For risk assessments the energy imparted would be the better quantity than the ESK. However, the data evaluation was performed with the data processing routines available at CDRH for the NEXT surveys, using ESK as the dose-related variable. Because intercomparison of techniques used in the two countries is one of the major objects of this study, it was decided to retain the ESK concept.

The distribution of the ESK values is shown in Fig. 5. The values for the United States were converted from ESE values using the numerical relationship that 1 mR corresponds to 0.0087 mGy. The shape of the distributions of the ESK values for grid technique is essentially equal in the two countries; however, the overall mean value of ESK in the United States is slightly lower than in Sweden.

Comparison of the United States and Sweden: interpretations and conclusions

The single variable that best reflects the variations of technique is the entrance skin air kerma. The mean value for the United States is 0.14 mGy and for Sweden 0.16 mGy. Part of the difference might be explained by the differences in the use of scatter suppression, which is used in 100% of the facilities in Sweden but only in 75% of the facilities surveyed in the United States. The use of a grid will increase the dose typically by a factor of 2–3. The average ESK value of the United States facilities using scatter suppression is 0.15 mGy, virtually identical with the average value for Sweden. This agreement may be coincidental, as shown by the following conclusions.

Variables in favour of lower ESK values in Sweden

The larger HVL values in Sweden due to higher tube voltage, more total filtration and absence of single phase units would lead to ESK values 25% lower in Sweden than in the United States. The over-processing conditions in Sweden (Fig. 4) would lower the ESK values another 10%.

Variables in favour of higher ESK values in Sweden

As seen from Fig. 3, the film–screen systems used in Sweden are significantly slower than those in the United States. It is impossible to predict precisely an accurate value of the impact of these differences on the ESK values, but it is likely to be ~20%.

Despite there being considerable differences in technique factors used, the ESK values in Sweden and the United States are almost identical for units using scatter suppression. This example shows that any comparison of techniques between different countries, regions or even facilities must include all relevant parameters if correct conclusions are to be reached.

The observed differences in techniques between the United States and Sweden may be explained as follows. The X-ray units in Sweden are all three-phase systems using high tube voltage techniques with scatter suppression. In the United States, there is a widespread use of lower tube voltage technique without scatter suppression. The processor speed indices give a hint of the greater emphasis in Sweden on quality control (QC) of the processor. In Sweden, the implementation of QC

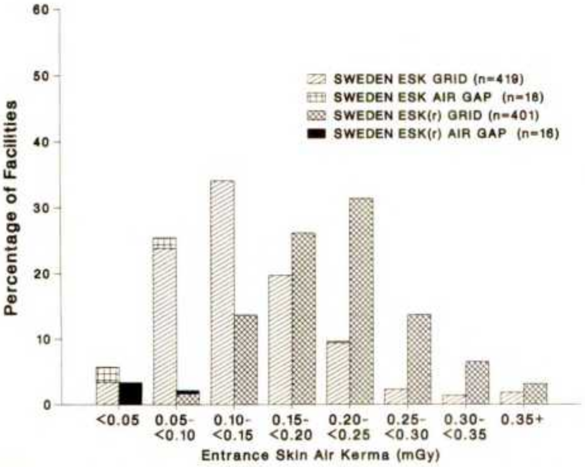

Figure 6. The distribution of air kerma values (ESK) and air kerma values normalized to 6 μGy air kerma at the film plane (ESK(r)) for PA chest examinations in Sweden.

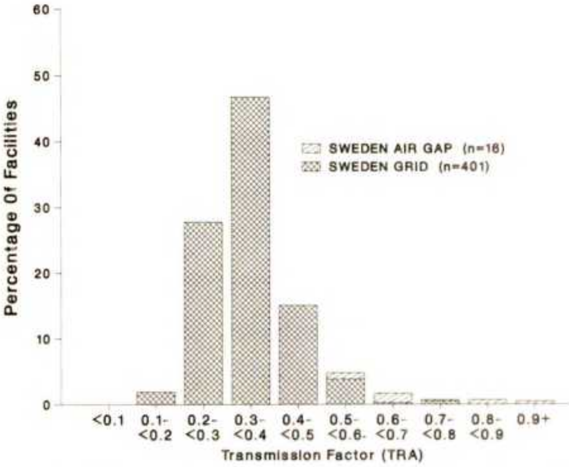

Figure 7. Measured transmission factors from the phantom exit to the entrance of the cassette for chest examinations in Sweden.

programmes became mandatory in 1983. Generally, film processor testing was the first step taken, and the figures for Sweden indicate the effectiveness of QC.

Other results in the Swedish survey

The additional measurements made in Sweden as a result of modification of the survey protocol allow the imaging chain to be subdivided into several component parts, from the X-ray tube to the completed radiograph. The absolute and relative influence of each of these components on the radiation dose can be easily evaluated.

Normalized ESK values

In order to exclude the influence of different film densities, the ESK values were normalized to a film density of 1.0 above base plus fog (ESK(s)). From the sensitometric test on the film used in the facilities, the normalization factors could be extracted taking advantage of the known relative exposures on the various steps of the step wedge. The average value of the ESK(s) is slightly lower than that of the ESK (0.14 and 0.16 mGy, respectively). However, the distributions are essentially the same, indicating that deviations in the exposure techniques resulting in a film density other than 1.0 above base plus fog do not have a major influence on the outcome of the survey.

In order to exclude the influence of the sensitivity of the different imaging systems, the ESK values were normalized to 6 μGy air kerma at the film cassette (ESK(r)). The normalization to 6 μGy was chosen because it corresponds to the average air kerma necessary to achieve a film density of 1.0 above base plus fog. Figure 6 shows the distribution of the ESK values together with that of the ESK(r) values. The distribution of ESK(r) is much narrower than that of the ESK indicating that one factor responsible for a large variation of the ESK values has been removed by this normalization. The ratio between the highest and the lowest value is 8.4. As seen in Fig. 6, the air gap units all have low ESK(r) values. For units using grids, the ratio between the highest and the lowest ESK(r) value drops to ~5. Large ESK(r) values are associated with grid misalignments in combination with low half-value layers.

Transmission from phantom exit to entrance film cassette (TRA)

The simultaneous measurement of the air kerma in front of the phantom (with the ionization chamber) and of the air kerma at the film cassette (indirectly with the calibrated reference cassette) gives values for the total transmission including the LucAl phantom.

The broad beam transmission through the phantom alone was measured for all the beam qualities involved in the survey. The combination of total filtration and tube voltage at which a certain HVL was obtained did not significantly affect the transmission. The transmission varied between 0.11 for an HVL of 2.5 mm Al and 0.27 for an HVL of 13 mm Al. The transmission from the exit point of the phantom to the entrance of the cassette can now be calculated using the ratio between the total transmission and the phantom transmission for a specific HVL.

For units using an anti-scatter grid, the transmission varied between 0.13 and 0.50, and the transmission for the units using air gaps varied between 0.5 and 1.0 (Fig. 7). Excluding units with verified errors in grid alignment, the lowest value is 0.25. This indicates that, for units using the same method of scatter suppression, the attenuation of the material between the patient and the film cassette varies by a factor of <2, including the variations caused by the different radiation qualities. However, because these values are relatively constant under normal circumstances, irregularities can be discovered by transmission measurements. Radiation exposure using an air gap will be roughly half that when using a grid, if all other parameters are constant.

Sensitivity of the imaging system (SEN)

The measured sensitivities (defined as the reciprocal value of the air kerma necessary to generate a film density of 1.0 above base plus fog) are in the range of 50–570 (mGy)$^{-1}$ with an average value of 160. Deviations by a factor of 1.5–2 (less sensitive) from the expected values, taken from literature or from manufacturers' information, were the rule rather than the exception. For some of the units, deterioration through aging of the screens is thought to be the reason for this disagreement.

Image quality

For the assessment of image quality, the radiographs of the imaging test device were evaluated with respect to high-contrast resolution, visibility of low-contrast objects and the presence of artefacts such as inhomogeneity of the optical density, stains or superposed grid structures.

As a consequence of the measuring geometry, the high-contrast resolution was determined mainly by the focal spot size. The resolution test pattern was placed within the LucAl phantom at a distance of 20 cm from the patient support. Ten per cent of the facilities showed resolution limts of <2 line pairs/mm.

The number of visible objects in the image was used as a quantification for the visibility of low-contrast objects. A somewhat arbitrary number was chosen as a limit for non-acceptance. Fifteen per cent of all facilities had values below this limit. The average of the ESK values was 0.15 mGy for the lowest acceptable number and reaches 0.19 mGy for the highest number.

Disturbing grid structures were observed at 20% of the facilities, just as much as for disturbing inhomogeneities in the optical density, and 25% of the facilities showed processor or film related artefacts such as stains, dirt and pressure marks on the film.

A slight positive correlation between the low-contrast visibility and the value for ESK was the only correlation seen between image parameters and dose. The material does not allow conclusions on a principal basis about minimum dose for the achievement of maximum image quality—too many variables are involved. An investigation with the aim of answering this question is in progress. The evaluation of radiographs of an anatomical phantom will suggest how the diagnostic image quality depends on the various techniques used and hence on the radiation dose.

Validity of the STEP procedure

In general, the results of the STEP procedure described the processing conditions well. However, in two specific circumstances the reliability of the method was found to be less valid.

The first occurred when processing conditions for Kodak T-Mat films were to be checked. There was evidence that changes in the processor conditions that would influence the performance of the reference film (Kodak X-Omat S) had little impact on the T-Mat film.

Secondly, several discrepancies were found in small table-top processors with shallow film immersion in the baths. Generally, the film used at the facility showed substantially better performance than the reference film with respect to sensitivity. Other film brands comparable to the reference film, *i.e.* blue sensitive films of RP type, showed similar sensitivities in "ordinary" processors, but as much as 50% higher sensitivity when processed in the table-top processors.

Summary and conclusions

Table I summarizes the results. In the last column, the

Table I. Compilation of the Swedish survey results

	Min	Max	Mean	ESK_{high}/ESK_{low}[a]
Tube voltage (kV)	100	150	133	—
Half-value layer (mm Al)	2.5	13	6	2.5
Exposure time (ms)	1.3	209	19	—
Film density	0.7	2.6	1.4	4.5
ESK[b] (mGy)	0.022	0.58	0.16	—
ESK(s)[c] (mGy)	0.020	0.70	0.14	—
ESK(r)[d] (mGy)	0.039	0.33	0.15	—
SEN[e] (mGy)$^{-1}$	50	570	160	11
Processor speed index	42	182	102	4.2
TRA[f]	0.13	1.0	0.36	7.5

[a] ESK_{high}/ESK_{low} = ratio between the highest and the lowest ESK values achieved when varying the identified parameter within the indicated range.

[b] ESK = air kerma free-in-air in the entrance plane.

[c] ESK(s) = ESK values normalized to net film density 1.0.

[d] ESK(r) = ESK values normalized to 6 μGy in the image plane.

[e] SEN = sensitivity of the imaging system expressed as the reciprocal value of the air kerma in the film plane resulting in net film density 1.0.

[f] TRA = transmission of the radiation beam from phantom exit to entrance of cassette.

relative dependency of the radiation dose on the identified parameter is indicated. It is given as the ratio ESK_{high}/ESK_{low} between the highest and the lowest ESK values that are achieved when varying the identified parameter within the range indicated, keeping all the other variables constant. The ratios give some indication of the effect the variation of a given parameter has on the radiation dose and, thus, efforts can be directed to those items having the largest effect.

Variations of the sensitivity of the film–screen combination give the largest variation in ESK, a ratio of 11. For film density, the factor is 4.5. However, the spread in densities obtained with the phantom measurements may not reflect the clinical variations, because the settings of the technique factors depend on what is regarded as a normal-sized patient, and that may differ from one facility to the other. The highest film density observed in the survey, 2.6, is certainly not relevant for clinical use. A more realistic upper limit for the film density of 2.0 would reduce the ratio of the associated ESK values from 4.5 to 3.

The radiation quality including tube voltage and filtration gives a ratio of 2.5 (deduced from the transmission measurements through the LucAl phantom). However, it must be emphasized that the ratio will be considerably lower when substituting the ESK values with values for the energy imparted, the quantity more closely related to the radiation risk.

Processing conditions account for a ratio of 4, indicating that film processing is a very crucial part in X-ray diagnosis.

The variations in attenuation of the material between the patient and the image receptor give a ratio of 7.5. However, as was pointed out above, when separating both methods of scatter suppression and disregarding the verified errors in grid alignment, a ratio of 2 is obtained for both methods.

It is evident that survey protocols should contain measurements of the sensitivity of the imaging system. Surveys with the purpose of determining corrective actions for the individual units should include all the variables listed in Table I.

Impact on future surveys

On the basis of the experiences gained in the Swedish survey, the following modifications of the current NEXT procedure are proposed. Two kinds of surveys are regarded: a "statistical" survey like the current NEXT protocol where the interest is mainly in the distribution of the radiation dose and some correlated parameters and an "investigational" survey with the aim of revealing the weak points of the individual units and correcting them. The programmes described below are realistic and cost effective and it should be possible to use them elsewhere.

Statistical survey

The current NEXT procedure is an example of such a survey. One minor extension is suggested: a sensitometer test on the type of chest film used by the facility giving the possibility of normalizing the ESK values to a specified film density. Measurements of the air kerma at the cassette using a reference cassette together with a reference film should be very useful. However, it is essential for the success of this method to maintain control of the properties of the reference system by means of rigid calibrations, which may be difficult to achieve when the method is in wide spread use.

Investigational survey

For this type of survey, it is essential to identify the weak points as precisely as possible. Corrective actions are most likely to be undertaken when it is clear what the fault is and how it is to be repaired. The protocol used in the Swedish study gives the results required and has proved to be practicable, and can be recommended for the conduct of investigational surveys.

Benefits of comparisons between countries

Countries such as Sweden and the United States have been involved in radiation protection for many years, usually developing their own techniques. It is apparent that whenever countries are working with similar goals, collaboration on more detailed areas, such as specific measurement techniques, would be beneficial to all. The Swedish and US collaboration has led to such a result: technology developed in the United States was modified and expanded for use in Sweden. The result has suggested ways of expanding and improving surveys conducted in the United States.

The comparisons have also revealed major differences in the performance of diagnostic procedures in the two countries. The United States should note the Swedish experience with regard to high tube voltage and filtration for chest examinations and the greater awareness of processor testing. Sweden should follow the United States lead in introducing faster film–screen systems. It is our hope that the results of this collaboration will stimulate both countries to take measures towards improved radiological procedures.

Acknowledgments

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Special thanks go to the hospital physicists and our colleagues at the NIRP engaged in the Swedish survey, who made it possible for the Swedish national survey of all chest units in the country to be completed within 1½ years. The Swedish part of this study was supported by grants from the National Institute of Radiation Protection (Project No. P-325).

References

BUNGE, R. E., DUCCA, A. T. & PROPERZIO, W. S., 1979. *Exposure in Chest Radiography: "NEXT" results. Optimization of Chest Radiography*, HHS Publication FDA 80-8124 (US Department of Health and Human Services, Food and Drug Administration, Bureau of Radiological Health, Maryland, USA).

BUTLER, P. F., CONWAY, B. J., SULEIMAN, O. H., KOUSTENIS, G. H. & SHOWALTER, C. K., 1985. Chest radiography: a survey of techniques and exposure levels currently used. *Radiology, 156*, 533–536.

CONWAY, B. J., BUTLER, P. F., DUFF, J. E., FEWELL, T. R., GROSS, R. E., JENNINGS, R. J., KOUSTENIS, G. H., McGROHAN, J. L., RUETER, F. G. & SHOWALTER, C. K., 1984. Beam quality independent attenuation phantom for estimating patient exposure from X-ray automatic exposure controlled chest examinations. *Medical Physics, 11*, 827–832.

SULEIMAN, O. H., SHOWALTER, C. K., KOUSTENIS, G. H. & HOTTE, E., 1982. *A Sensitometric Evaluation of Film-Chemistry Processor Systems in the State of New Jersey*, HHS Publication FDA 82-8189 (US Department of Health and Human Services, Food and Drug Administration, Bureau of Radiological Health, Maryland, USA).

1990, *The British Journal of Radiology*, 63, 41–50

The response of the pig lung to fractionated doses of X rays

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Abstract. A radionuclide ^{133}Xe clearance technique has been used to assess changes in the regional gas exchange capacity of the lung after the irradiation of part of the lung of pigs with fractionated doses of 250 kV X rays. Changes in the gas-exchange capacity of an irradiated volume of lung were compared with a similar volume of unirradiated lung in each animal. The results from the lung function tests were converted into quantal data on the basis of the percentage of lung function tests in animals showing a $\geqslant 15\%$ impairment of function in the irradiated lung compared with contralateral unirradiated lung in the same animal. From those quantal data, ED_{50} values ($\pm$SE) were obtained for each fractionation schedule. These ED_{50} values were used to determine time–dose–fractionation relationships for both early and late radiation-induced damage to the lung. There was apparently no recovery phase between the early and late phases of damage to the lung. In general, ED_{50} values for the late effect were slightly lower than those for the early effect, but this only proved significant when measurements obtained at 4 weeks after treatment were included. Varying the period for the assessment of early and late damage did not have a major effect on the results but did suggest that late damage was established in pigs by 39 weeks after irradiation. The linear-quadratic model did not provide a satisfactory fit to the fractionation results for pig lung. However, a modified nominal standard dose equation did provide a better description of the findings. A value of 0.44 ± 0.06 was obtained for N exponent in the equation for both early and late lung damage when the single-dose data points were included in the analysis. The value of the N exponent was increased to 0.52 ± 0.08 when the single-dose data were excluded. This increase was not significant.

The results of several previous studies have shown a clearly defined relationship between radiation dose and the development of lung damage (Prato et al, 1976; van Dyk et al, 1981; Mah et al, 1987; Rezvani et al, 1989). The time of onset and the severity of radiation-induced damage to lung depend on the total dose and the dose/fractionation schedule. The dose–response relationship for the incidence of radiation-induced damage to lung was very steep (Mah et al, 1987; Rezvani et al, 1989) and thus an accurate knowledge of the above factors is required to establish safe "lung tolerance" doses for patients. An accurate assessment of the relationship between total dose, overall treatment time and the number of fractions, or dose per fraction, cannot for ethical reasons be obtained from systematic studies on patients; hence this information must come from experimental studies on animals. These results can then be compared with the limited data obtained from human studies.

Studies of time–dose–fractionation relationships in mouse and pig lung have all pointed to the major importance of the fraction number N, and hence the fraction size, in the determination of isoeffect doses for the lung. The results, which were mainly obtained from the studies of radiation pneumonitis, suggested a value of between 0.32 and 0.46 for the N exponent in a modified nominal standard dose (NSD) equation (Ellis, 1968). The exponent relating to overall treatment time, T, was relatively small, ranging from 0.05 to 0.07 (Wara et al, 1973; Field et al, 1976; Moustafa & Hopewell, 1977; Herrmann et al, 1986). On the basis of clinical data (Wara et al, 1973), a value of 0.41 was obtained for the N exponent for human lung.

Based on the assumption of the validity of the linear-quadratic (LQ) model of cell survival and the concept of target cells, the values for the α/β ratio quoted for lung after photon irradiation have ranged from 2.38 to 5.75 Gy (Travis et al, 1983). Parkins et al (1985) have also studied radiation-induced lung damage at later times after irradiation as well as the pneumonitic period. Using a breathing rate assay, these authors obtained similar α/β ratios and did not observe any significant difference in the α/β ratios for early (28 weeks) and late (68 weeks) radiation-induced damage to the lung. However, using lethality as an end-point, three out of a total of six analyses showed a significant difference between the α/β ratios for early and late lung damage.

The objective of the present study was to determine time–dose–fractionation relations for both early and late radiation-induced damage to the lung. It has been suggested (Down, 1986) that the mouse is not a good model to study the late effects of radiation on the lung, because the later functional changes measured in some strains of mice could be due to pleural effusion rather than radiation-induced damage to the lung. On the other hand, the results of recent studies in the pig (Rezvani et al, 1989) indicate that late radiation changes, comparable to those seen in man, do develop in this animal model after $\geqslant 39$ weeks. In addition, there are a number of anatomical similarities between pig and human lung (McLaughlin et al, 1961), perhaps making it an ideal model for man. Irradiation involved only part of the total lung volume, and since there was no definitive time of demarcation between the early and later phases of lung damage, the influence of varying the early/late times of assessment on the fractionation relationship and their interpretation has been investigated.

Materials and methods

Sixty-six female pigs of the Large White strain were used in these investigations. Animals were brought into the Animal House when they were approximately 12 weeks old (weight 20–25 kg), and they were allowed an acclimatization period of at least 2 weeks before any experimental procedures were undertaken.

Prior to irradiation, the position of the fully ventilated basal lobe of the left lung was determined fluoroscopically and included in a 10 cm × 20 cm field tattooed on the overlying skin. In each animal this field was irradiated with either 6, 14, 18 or 30 fractions of 250 kV X rays given in either 5, 18 or 39 days (Table I) at a dose rate of 0.69 Gy/min from a machine operating at 15 mA, with 0.5 mm Cu and 1 mm Al added filtration half-value layer (HVL) (1.4 mm Cu). For irradiation, the rectangular field was reduced to a triangular shape by a cut-out in 4 mm lead placed on the surface of the skin. A Perspex-ended applicator was used with a focus–skin distance (FSD) of 50 cm. The quoted doses refer to those at the centre of the irradiated lobe of the lung, which were corrected to allow for the low density of lung tissue. The irregular shape of the lung tissue irradiated resulted in a maximum variation in dose, across the fully ventilated lung, of ~24%. However, average lung dimension suggested that an ~12% variation in total dose across the lung was more representative.

All procedures were carried out with the animals under anaesthesia, which was maintained with a 2% halothane, ~30% nitrous oxide and ~70% oxygen mixture. Animals were intubated and a closed, non-rebreathable system was used for the irradiations and the subsequent functional studies.

Lung-function tests were performed prior to irradiation at 4 and 13 weeks, then at 13-weekly intervals until 104 weeks after the midpoint of irradiation for the 18-day and 39-day irradiation schedules. Each animal was tested twice on each occasion using the following standard procedure: 1–5 mCi (depending on the size of the animal) of ^{133}Xe in saline (10 mCi/ml) was injected as a bolus via an ear vein. The accumulation and clearance of the ^{133}Xe from comparable areas of the irradiated and unirradiated lung in the same animal was recorded using two matched, collimated, NaI scintillation detectors. These were connected to a Nokia LP4840 multichannel analyser. Activity counts against time were integrated over intervals of 0.4 s and were collected for a total of 160 s. Prior to each functional assessment the position of comparable areas of the left and right lung were established using X-ray fluoroscopy.

The time–activity curves obtained were normalized by taking the peak activity over each lung as 100%. The clearance part of the time–activity curve for each lung was then analysed using a two-compartmental model (Rezvani & Hopewell, 1986). From each time–activity curve, the rate constant for the clearance of ^{133}Xe, which represented the gas exchange capacity of that lung, was obtained. Changes in the function of the irradiated lung were assessed as a "functional index", obtained by the comparison of the rate-constant obtained for the irradiated lung with that of the unirradiated lung in the same animal. In order to convert these quantitative measurements into quantal data, a threshold level of impairment in lung function of ⩾15% was set for the variation in the function of the irradiated left lung with respect to the unirradiated right lung in the same animal. A ⩾15% threshold level of effect was selected because a 15% impairment of lung function was the minimum significant difference that could be detected between the irradiated and unirradiated lung in the same animal. Any lung that had a functional index of ⩽85% was considered to be affected. The number of lung-function tests in animals showing a response versus the number of tests performed on animals in each dose group were scored and classified into different groups according to the time scale after irradiation, *i.e.* 4–26 weeks for early (pneumonitic) and 39–104 weeks for the late (fibrotic) effects. These quantal data were analysed by probit analysis (Finney, 1964) and ED_{50} (±SE) values obtained. In order to assess the influence of different assay times the data were also grouped over 13–26 weeks, 4–39 weeks or 13–39 weeks for early

Table I. ED_{50} values (±SE) for a ⩾15% reduction in lung function for different fractionation schedules obtained for various assessment times

Fractionation schedule	Times of assessment (weeks)						
	4–26	4–39	13–26	13–39	39–65	39–104	52–104
Single dose	9.68±0.30	9.72±0.30	10.12±0.33	9.89±0.35	9.03±0.47	9.73±0.34	9.84±0.31
6F/5d	20.36±3.41	19.23±2.30	15.02±3.22	15.24±2.15	16.96±1.48	16.79±1.42	16.00±2.04
6F/18d	21.54±3.09	25.70±3.23	17.19±2.46	18.64±1.75	17.32±1.34	15.71±1.43	13.38±2.97
14F/18d	32.91±2.54	31.74±2.99	28.91±1.96	27.02±2.22	24.86±3.48	27.17±1.97	24.88±2.72
6F/39d	21.23±5.48	22.82±4.09	22.53±4.13	23.02±1.89	17.04±2.44	17.13±2.64	16.93±2.99
14F/39d	37.95±3.48	31.51±2.85	27.55±3.08	26.16±2.40	24.22±2.10	22.64±1.72	22.11±1.88
18F/39d	40.22±4.53	38.30±2.70	40.63±3.05	36.78±2.59	25.64±3.48	29.25±2.77	28.66±3.16
30F/39d	51.20±4.59	45.29±4.08	45.29±3.95	41.61±2.24	38.46±3.11	38.11±2.50	38.28±2.19

changes and 39–65 weeks or 52–104 weeks for the study of late effects.

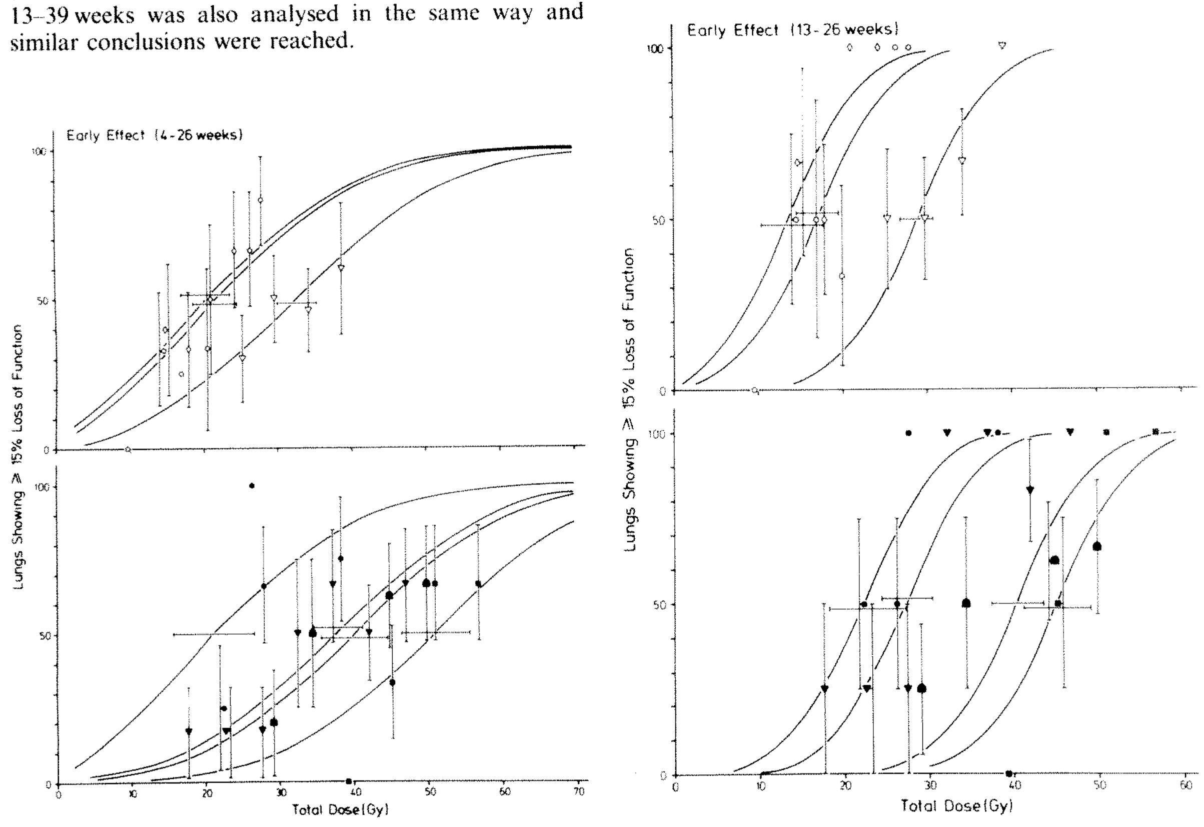
Results obtained after irradiation with single doses of ^{60}Co γ rays (Rezvani et al, 1989) were analysed further and a relative biological effectiveness (RBE) of 1.0 was used for ^{60}Co γ rays. Down (1986) has shown no measurable differences between the effects of ^{60}Co γ and 250 kV X irradiation for mouse lung.

Results

Curves showing the dose-related changes in the incidence of lung function tests showing a $\geqslant 15\%$ reduction in function are shown in Fig. 1. The data are based on the accumulation of results for two early time periods: 4–26 weeks and 13–26 weeks after irradiation. The sparing of lung damage with smaller dose/fraction for fractions given in the same overall treatment time is illustrated by the displacement of the dose–effect curves to the right with increasing fraction number. The dose–effect curves based on the results obtained between 4 and 26 weeks after irradiation (Fig. 1a) were shallower than those obtained from the assessments that included the later time period of 13–26 weeks (Fig. 1b). The incidence of lung-function tests in animals showing a $\geqslant 15\%$ loss of function between 4–39 weeks and 13–39 weeks was also analysed in the same way and similar conclusions were reached.

The dose–response curves for the incidence of lung function tests in animals showing $\geqslant 15\%$ loss of function at later periods, *i.e.* 39–104 weeks or 52–104 weeks after irradiation, are shown in Fig. 2. For these later periods, the sparing of lung damage was also greater for small doses per fraction for fractions given in the same overall treatment time.

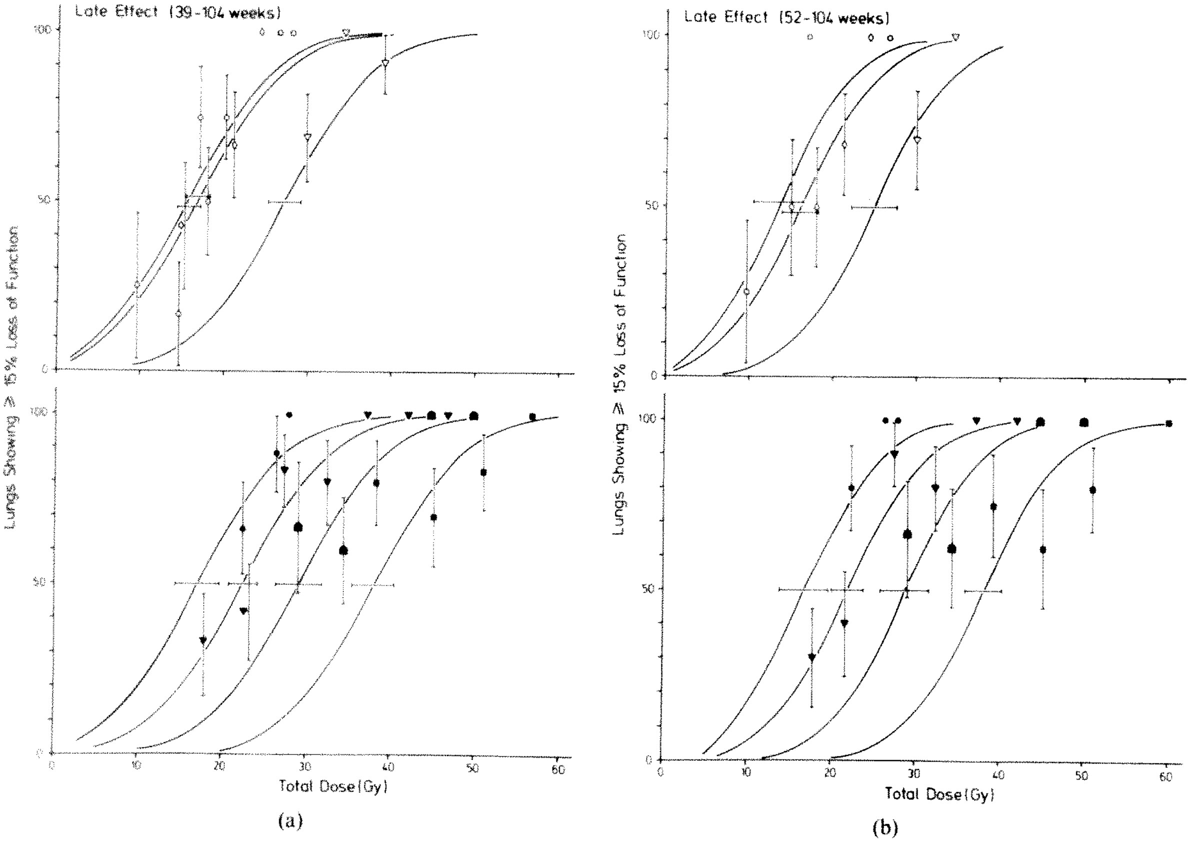
The ED_{50} values for the different fractionation schedules and for the various time periods of evaluation are summarized in Table I. The ED_{50} values for the assessment periods of 13–26 weeks and 13–39 weeks were lower than those for 4–26 weeks and 4–39 weeks but did not prove to be significantly different ($p > 0.05$) except for the 14F/39d group ($p < 0.05$). For the later assessment times, $\geqslant 39$ weeks after irradiation, the ED_{50} values were again lower. However there was no significant difference between the ED_{50} values obtained for the assessment periods of 39–65 weeks, 39–104 weeks and 52–104 weeks ($p > 0.05$). This would imply that late radiation-induced damage to the lung in the pig might become fixed at 39 weeks after irradiation. Perhaps the results obtained at 39 weeks should not be considered an appropriate time after irradiation for inclusion as an early effect.



(a)

(b)

Figure 1. Dose–effect curves of the incidence of lung function tests in animals showing a $\geqslant 15\%$ loss of function for total doses given as: 6F/5d (◇), 6F/18d (○), 14F/18d (▽), 6F/39d (●), 14F/39d (▼), 18F/39d (▲), 30F/39d (■). Assessment was between (a) 4 and 26 weeks or (b) 13 and 26 weeks after the midpoint of irradiation. Error bars indicate ±SE.



(a)

(b)

Figure 2. Dose–effect curves of the incidence of lung function tests in animals showing a ≥15% loss of function for total doses given as: 6F/5d (◇), 6F/18d (○), 14F/18d (▽), 6F/39d (●), 14F/39d (▼), 18F/39d (⬟), 30F/39d (■). Assessment was between (a) 39 and 104 weeks or (b) 52 and 104 weeks after the midpoint of irradiation. Error bars indicate ±SE.

The ED_{50} values for early (4–26 weeks) and late (39–104 weeks) effects were not significantly different after irradiation with single doses and the 6F or 14F in 18-day treatment schedules. Those for 14, 18 and 30F in 39 days were significantly different ($p<0.05$). However, when the ED_{50} values for the 13–26 week interval were compared with those for late effects (39–104 weeks) the only significantly different values were those of the 18F/39-day treatment group. This suggests that the lung function measurements at 4 weeks play an important role in the determination of the ED_{50} values. However, no marked dose-related damage was observed at 4 weeks after fractionated irradiation and overall, the impairment of lung function occurred progressively between 4 and 13 weeks after irradiation.

Log–log plots of the isoeffective ED_{50} values versus the number of fractions for early and late effects, assessed at different time periods after irradiation, are given in Fig. 3. The possible effects of overall treatment time have been ignored in these calculations. In any event, the ED_{50} values obtained for a specific number of fractions, with different overall treatment times, were not significantly different (Table I). Thus, a single regression line was fitted regardless of overall treatment time. The lines were fitted with and without the inclusion of the single-dose data points. The slopes of the fitted lines, which represent the values of fractions exponent N are listed in Table II. When the single-dose data points were included, the values of N ranged from 0.4 to 0.5 and there were no significant differences, no matter what time of assessment was selected. Therefore, a common exponent of N of 0.44 ± 0.06 could be adopted for both early and late radiation-induced damage to the lung. Exclusion of the single-dose data points resulted in a general increase in the size of the N exponent. However this was not significant for either the individual values or the group mean values. Therefore, a common exponent of N of 0.52 ± 0.08 could be adopted on the basis of this analysis.

Log–log plots of the isoeffective ED_{50} values versus overall treatment time for both early and late radiation-induced damage, assessed at different time periods after irradiation, are given in Fig. 4. The ED_{50} values for doses given as 6 or 14 fractions in the same overall treatment time were significantly different from each other and thus separate regression lines were fitted to

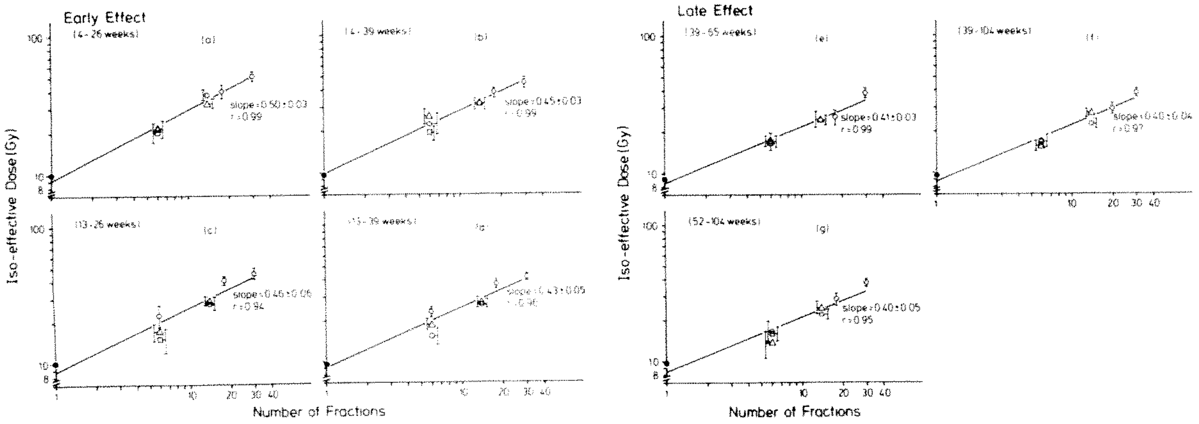


Figure 3. Log–log plot of the ED$_{50}$ values (±SE) for a ≥15% reduction in lung function against number of dose factions, N, assessed between 4 and 26 weeks (a), 4 and 39 weeks (b), 13 and 26 weeks (c), 13 and 39 weeks (d), 39 and 65 weeks (e), 39 and 104 weeks (f) and 52 and 104 weeks (g) after the midpoint of irradiation. Doses were given in 5 days (□), 18 days (△), 39 days (○) or as a single dose (●).

the 6F and 14F data. The slopes of the fitted lines and their errors are listed in Table III. The 14F results consisted only of two data points and hence no errors could be obtained for the slopes of the regression lines fitted to these findings. Thus, the confidence that could be attached to the values of these time exponents was limited. For the early assessment times the values of T exponent obtained on the basis of 6F data varied from 0.023 to 0.196. However, only the slopes of the lines fitted to data points assessment at 13–26 weeks and 13–39 weeks were significantly different from zero ($p<0.05$). A common exponent of T of 0.126±0.056 could be considered for early radiation-induced lung damage. This slope was significantly different from zero ($p<0.05$). The comparable common slope obtained on the basis of 14F data was 0.018±0.050, which was not significantly different from zero ($p>0.5$).

The slopes of regression-line fits for late radiation-induced reactions assessed at different time-periods for the 6F data ranged from 0.004 to 0.011 (Table III). None of these values was significantly different from zero, neither were the common slopes obtained from the 6F and 14F data significantly different from zero, $p>0.5$ and $p>0.1$, respectively. This implies that the overall treatment time had no effect on the expression of late radiation-induced damage to the lung.

Table II. Slopes (±SD) of regression line fits to log–log plots of the ED$_{50}$ values for the impairment of lung function in the pig against number of radiation dose fractions (N) for different assessment times

Time of assessment (weeks)	Individual and group values of the exponent N		
With single dose			
4–26	0.50±0.03	0.46±0.09	0.44±0.06
4–39	0.45±0.03		
13–26	0.46±0.06		
13–39	0.43±0.05		
39–65	0.41±0.03	0.40±0.09	
39–104	0.40±0.04		
52–104	0.40±0.05		
Without single dose			
4–26	0.57±0.04	0.53±0.11	0.52±0.08
4–39	0.44±0.06		
13–26	0.60±0.10		
13–39	0.51±0.09		
39–65	0.45±0.07	0.50±0.10	
39–104	0.51±0.04		
52–104	0.56±0.06		

All values of N were significantly different from zero ($p<0.001$).

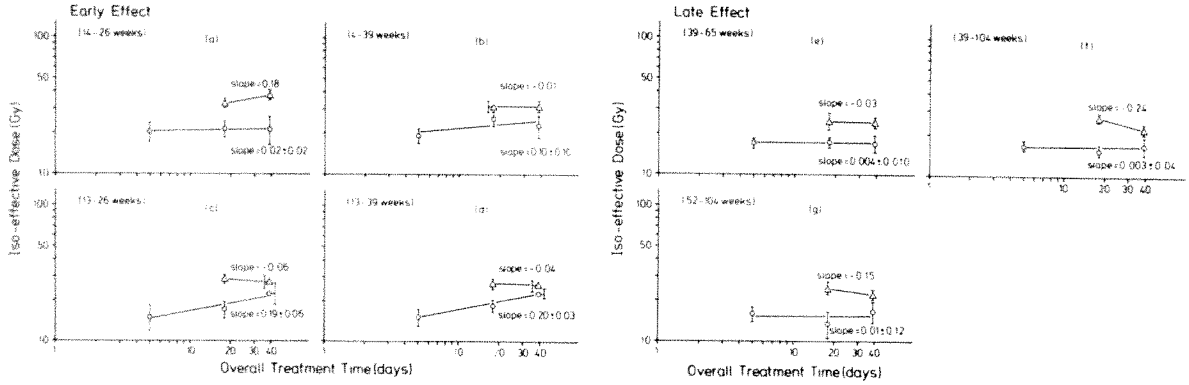


Figure 4. Log–log plot of the ED_{50} values ($\pm$SE) for a $\geqslant 15\%$ reduction in lung function against the overall treatment time, *T*, assessed between 4 and 20 weeks (a), 4 and 39 weeks (b), 13 and 26 weeks (c), 13 and 39 weeks (d), 39 and 65 weeks (e), 39 and 104 weeks (f) and 52 and 104 weeks (g) after the midpoint of irradiation. Doses were given in 6 (○) or 14 (△) fractions.

Plots of the reciprocal of the ED_{50} isoeffective dose against the dose per fraction (Fe-plots) for the early (4–26 weeks) and late (39–104 weeks) assessment times for lung damage are shown in Fig. 5. Linear regression lines were fitted both with and without including the single-dose data. When the same procedure was applied to the data obtained from the other assessment times, there was a general trend for an improvement of the fit when the single-dose data were included. The α/β ratios obtained from these plots and similar analyses for other early and late assessment times are listed in Table IV. In the majority of instances the inclusion of the single-dose data had a significant effect on the value of the α/β ratio: inclusion of single-dose data significantly increased the value of that ratio. When the single-dose data were excluded, the α/β ratio was only significantly greater than zero for the 39–65 weeks assessment period. Inclusion of the single-dose data resulted in α/β ratios significantly greater than zero in six out of seven instances (Table IV).

The same isoeffect data shown in Fig. 5 have also been assessed according to the method proposed by

Table III. Slopes ($\pm$SD) of linear fits to log–log plots of the ED_{50} values for the impairment in lung function against overall treatment time (*T*) for different assessment times obtained for both the 6F and 14F irradiation groups

Time of assessment (weeks)	Variation in the exponent of *T* with fraction number	
	6F	14F
4–26	0.023 ± 0.017	0.184
4–39	0.098 ± 0.101	−0.009
13–26	0.188 ± 0.065[a]	−0.062
13–39	0.196 ± 0.031[a]	−0.042
(Early assessment times)	0.126 ± 0.056[a]	0.018 ± 0.05
39–65	0.004 ± 0.010	−0.034
39–104	0.004 ± 0.043	−0.238
52–104	0.011 ± 0.118	−0.153
(Late assessment times)	0.006 ± 0.03	−0.14 ± 0.095

[a]Values significantly different from zero ($p < 0.05$).

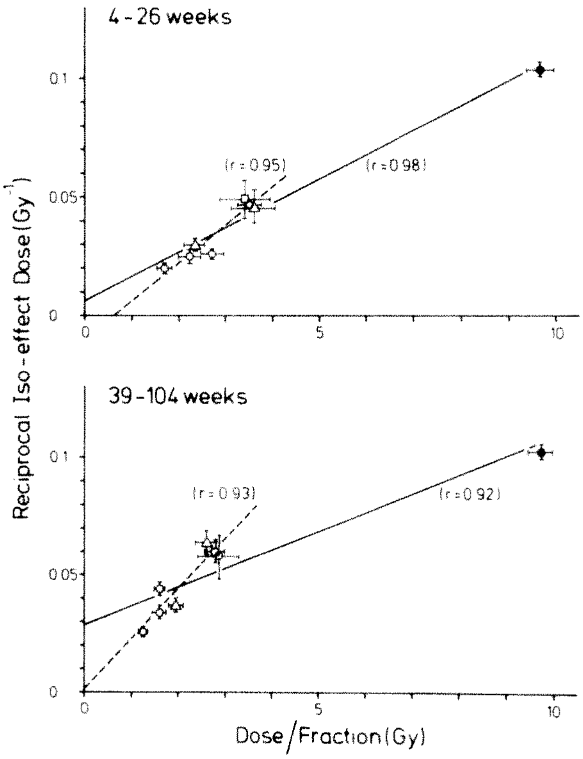


Figure 5. Plots of $1/ED_{50}$ values ($\pm$SE) for a $\geqslant 15\%$ reduction in lung function for early effect (4–26 weeks) and late effect (39–104 weeks). The regression fit was either through all data points (——) or excluded the single dose point (- - -). Doses were given in 5 days (□), 18 days (△), 39 days (○) or as a single dose (●).

Table IV. Variation in α/β ratios ($\pm$SD), obtained from an Fe-plot, for radiation-induced lung damage assessed at different times after irradiation. The vertical intercept of the regression lines fitted to $D_n - D_m$ versus $D_m d_m - D_n d_n$ plots (Tucker test) are also listed

Time of assessment (weeks)	Method of analysis			
	Fe plot		Tucker test	
	With single dose (α/β)	Excluding single dose (α/β)	With single dose (y-intercept)	Excluding single dose (y-intercept)
4–26	0.60±0.40	−0.63±0.44	−14.75±2.34[a]	−9.21±2.81[a]
4–39	0.90±0.41[a]	1.63±1.28	−11.94±1.91[a]	−9.68±1.89[a]
13–26	2.75±1.21[a]	1.00±1.98	−14.19±1.96[a]	−10.95±2.60[a]
13–39	2.75±1.11[a]	1.80±1.93	−12.28±1.63[a]	−10.88±1.88[a]
39–65	2.5 ±0.47[a]	0.59±0.25[a]	−7.74±1.84[a]	−8.15±1.85[a]
39–104	3.63±0.88[a]	0.10±0.38	−9.01±1.87[a]	−8.19±1.67[a]
52–104	4.86±0.35[a]	0.09±0.72	−9.87±1.77[a]	−7.34±1.81[a]

[a] Values significantly different from zero at the 5% level.

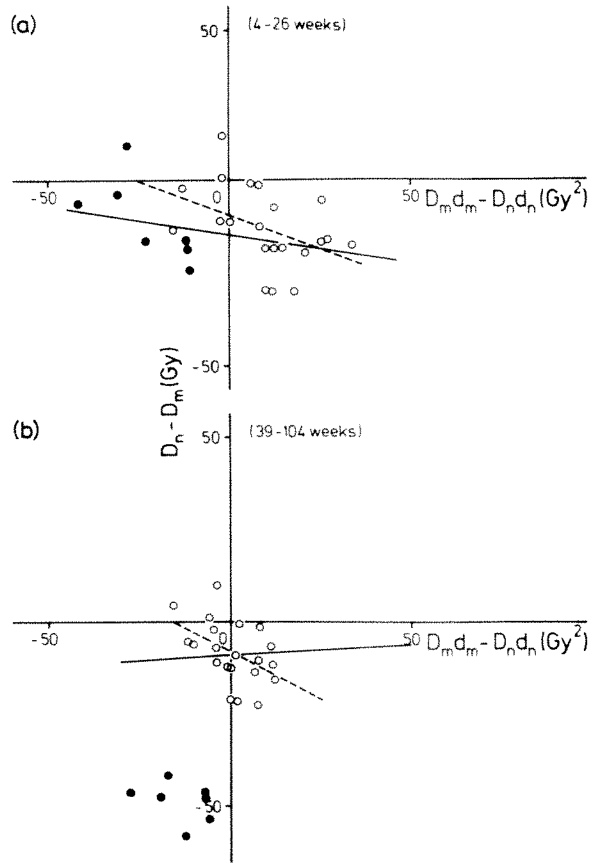


Figure 6. Plots of $D_n - D_m$ against $D_m d_m - D_n d_n$ for a $\geqslant$15% reduction in lung functions for (a) early effect (4–26 weeks) and (b) late effect (39–104 weeks). The regression fit was either through all data points (●—○) or excluded the single dose point (○- - -○).

Tucker (1984). These findings are presented in Fig. 6. A regression fit to the data points for an early assessment period (4–26 weeks) intersects the vertical-axis at −14.75±2.34 Gy. The comparable regression line fitted through the data for the late assessment period (39–104 weeks) intersects the vertical-axis at −9.0±1.87 Gy. The results of this analysis and those obtained from similar analyses of all the other assessment periods are also listed in Table IV. The vertical-intercepts were significantly different from zero ($p<0.01$) in all cases. Inclusion or exclusion of the single-dose data did not alter this result. On the basis of the LQ model, a regression line based on Tucker's test should pass through the origin in such plots.

Discussion

Previous results obtained after the irradiation of pig lung with single doses of ^{60}Co γ rays (Rezvani et al, 1989) have shown that there was a marked reduction in the function of the lung at 4 weeks after irradiation. This impairment was not dose-dependent but was followed by a persistent dose-dependent reduction in lung function after doses of >9 Gy. This marked early reduction in lung function was not seen in the studies with fractionated doses. This suggests that fractionated irradiation may spare a very early exudative phase of damage. Alternatively, as the duration of the treatment time was long compared with the time of the first assessment, *i.e.* 4 weeks from the midpoint of the irradiation, the peak of this early phase of damage to the lung may have been missed. In this respect it is of interest to note that the ED_{50} values for fractionated irradiation regimes given in 39 days, assessed for the early time period (4–26 weeks), were significantly different from those assessed later, at 39–104 weeks. This difference might be due to the influence of the 4-week time point, *i.e.* 1 week after the completion of irradiation, because when the ED_{50} values for the alternative early period (13–26 weeks) were compared with the ED_{50} values for the late assessment time

(39–104 weeks), there was no significant difference between the ED_{50} values for early and late damage, except for 18F/39 days. No significant differences between the ED_{50} values for any early and late assessment period were found for the 18-day irradiation schedules: 4 weeks was ~3 weeks after the end of treatment. On the basis of these findings it would seem most appropriate to consider 13–26 weeks as the best time period for the assessment of early radiation-induced damage to pig lung.

From the general similarity in the ED_{50} values for early (13–26 week) and late ($\geqslant$39 week) reactions it can be concluded that the late damage might be a continuation of the earlier damage. This finding is consistent with earlier observations after single (Rezvani et al, 1989) and fractionated doses of irradiation (Herrmann et al, 1986) in the pig. The latter authors assessed radiogenic reactions from 8 to 43 weeks after hemithorax irradiation and found no significant difference in the ED_{50} values for early and late times. There was no significant difference either between the isoeffect doses for mice assessed at 28, 48 and 68 weeks after thoracic irradiation (Parkins et al, 1985; Parkins & Fowler, 1985). However, these observations are incompatible with those of Travis and Down (1981), who showed a clear dissociation between early and late radiation-induced damage in mouse lung. The studies of Travis and Down (1981) were based on monitoring the breathing rate after irradiation, and it has subsequently been shown by one of these authors (Down, 1986) that the mouse is not a good model in which to study late radiation effects on the lung. In particular, the later increase in breathing rate in the strain of mice initially used by these authors could be due to pleural effusion rather than to radiation-induced damage to the lung. On the other hand it is possible that the dissociation of early and late damage might occur only at a specific dose level. In pigs, the similarity of the ED_{50} values for assessment times of 39–65 weeks and 39–104 weeks suggests that late damage was almost established by 39 weeks after irradiation.

There has been much discussion of the range of applicability of the LQ model (Barendsen, 1977; Fisher & Hendry, 1988), and it has been suggested that its application should be limited to the lower dose region, $\leqslant$8 Gy per fraction. Thus, on the basis of this suggestion, inclusion of the single-dose data in the analysis of the present lung study could bring about a significant deviation from the predictions of the LQ model. However, the α/β ratios, obtained from Fe-plots that included only the fractionated irradiation data, were not significantly different from zero for both the early and late effects at all assessment times except for 39–65 weeks after irradiation. In contrast, inclusion of the single-dose data had a considerable effect on the value of the α/β ratios obtained from these Fe-plots; values were now significantly greater than zero. The values of the α/β ratio obtained using this method of analysis were within the range reported for mouse lung by Travis et al (1983) and Parkins et al (1985) using increased breathing rate and death from radiation-induced injury to the lung. Single-dose results were included in the derivation of the α/β ratios by both sets of authors. Similar effects after inclusion of the single-dose data have been observed for liver cells, where it appeared that inclusion of the single-dose data in the Fe-plots made the regression lines shallower and this increased the values of the α/β ratio considerably (Fisher & Hendry, 1988).

It has also been proposed that incomplete repair during the interfraction intervals was a factor responsible for the divergence from linearity of Fe-plots (Thames et al, 1984; Thames 1985). Deviation from the LQ model for mouse lung data was explained on the basis of monoexponential repair kinetics with a half-time for repair of 1.5 h (Thames et al, 1984). The shortest interfraction time interval used in the present studies with pigs was 24 h. This suggests that incomplete repair is unlikely to describe the deviation from the LQ model observed in these studies.

For the kidney, it has been demonstrated (Lebesque et al, 1986) that the LQ model was only applicable for fraction numbers >16 and that it was inadequate for explaining the effects after larger doses per fraction. These authors appeared to rule out the possibility that incomplete repair might explain this finding. However, since a minimum time interval of 5 h was used by these authors, it could be argued that incomplete repair did play a part in their experiments. The authors demonstrated that the α/β ratio obtained for small dose fractions (*i.e.* 16, 32 and 64 fractions) was different than that found for all data *i.e.* including larger doses per fraction. Ang et al (1985) also reported higher α/β ratios for smaller doses per fraction for the rat spinal cord.

In the present studies with pigs, the significant y-intercept and the scatter of the data points when the results were assessed by the method proposed by Tucker (1984), suggest that the LQ model is not adequate for describing the radiation effects on the function of a complex organ such as the lung. This model is based on the assumed cell-survival characteristics of a single target-cell population, not on the function of a complex organ, which depends on more than one cell type. The survival characteristics of these cells might individually be considered to behave according to the LQ model, but their collective survival characteristics and the eventual function of the organ are more complex. In fact, the question of what the target cell population for the lung is, is still a matter of debate. In mice, it has been shown (Ulrich & Meyer, 1982) that the proliferation of Type II pneumocytes was increased considerably 2 days after the administration of butylated hydroxytoluene (BHT). Over this time period it was found that the lung was the most sensitive to radiation and hence they concluded that Type II cells were the target cell population. However, BHT treatment at this time accelerated the development of pneumonitis, suggesting that the apparent increased radiosensitivity of lung 2 days after BHT treatment might be due to an independent mechanism of cell kill. On the other hand, there is considerable evidence to indicate that damage to macrophages, endothelial cells, disturbance in the endothelial cell function and changes in capillary permeability could be the determining factors in the response of lung to irradiation (Johnson et al, 1970; Gross, 1978, 1981; Ts'ao et al, 1983a, b; Ward et al, 1983; Law et al, 1986).

A modified NSD formula appears to provide a better fit to the data obtained for the response of pig lung to fractionated irradiation. The values of the N exponents for "early" and "late" lung damage were not significantly different, and common values of 0.44 ± 0.06 and 0.52 ± 0.08 were obtained when the single-dose data points were included or excluded from the analysis, respectively. These values were comparable to the value of 0.41 proposed for human lung (Wara et al, 1973), and also within the range of values reported by different authors from the results of experimental studies on animals (Wara et al, 1973; Field et al, 1976; Parkins et al, 1985; Herrmann et al, 1986). Parkins et al (1985) reported a lower value of 0.33 for fraction numbers of 5–20. However, with a short interfraction interval of 6 h for a 20F/12d schedule, the effects of incomplete repair could have been underestimated and the actual value for the N exponent reduced. In the analysis of the present results for pig lung, any effects of overall treatment time were ignored in the evaluation of the size of the N exponent. However, this is likely to be unimportant since time was only a significant factor for "early" lung damage for treatments given in six fractions, and then only for the assessment intervals of 13–26 weeks and 13–39 weeks.

The T exponents for late damage to pig lung, obtained from the results of the present study, were not significantly different from zero. For "early" damage there was a time factor that was significantly greater than zero in the case of the 6F results (0.126), but not for 14F. However, if the results for 6F and 14F averaged, a smaller value, within the range 0.05–0.07, was obtained. This is in keeping with average values reported by others for studies in experimental animals (Wara et al, 1973; Field et al, 1976; Herrmann et al, 1986) and for man (Wara et al, 1973). The data from the pig lung indicates that value of the T exponent varies with the fraction number and therefore this kind of averaging must be considered with caution. This suggestion is also supported by the finding that when the time-related correction factor (γ/β), as proposed by Travis and Tucker (1987), was applied to the present 6F data, assuming a generally accepted value for α/β of 3 Gy, a value of 2.1 ± 0.3 Gy^2/day was obtained. This is similar to the value of 2.2 Gy^2/day obtained by the above authors for mouse lung, but this is not surprising since these calculations were dominated by the data from Field et al (1976), whose experiments were predominantly with 2F and 5F.

Application of this approach to the present 14F data produced no significant time-related correction factor. A similar difference in the effects of overall treatment time with different fraction numbers, as reported for pig lung has also been reported for acute reactions in pig skin where there was a significant time factor after 6F of X rays, between 18 and 39 days, but not after 14 fractions (Hopewell et al, 1988). This difference was attributed to the counteracting effects of cell repopulation and the redistribution of cells within the cell cycle.

The presence of a time factor for radiation-induced pneumonitis in mouse lung was first attributed to repopulation of the lung tissue (Field & Hornsey, 1974), but later it was suggested that it was due to a "slow" repair process (Field et al, 1976). This was analogous to, but not continuous with, "Elkind" repair. The "slow" repair process could be stopped by cell division and therefore it could be observed in slowly dividing, late-responding tissues but not in rapidly proliferating, acute responding tissues. If this were true then an equal, if not greater, time factor would be expected for late radiation-induced lung damage, compared with early damage. The results of the present studies are not in keeping with the suggestion, since the T exponents for late assessment times were not significantly different from zero.

In summary, the present findings in the pig suggest that a modified NSD formula is a better method of expressing the effects of fractionated irradiation on lung tissue. In such an equation, a common exponent of N of 0.44 was equally applicable for early and late radiation-induced damage to the lung. However, the time exponent T was found to depend on the type of effect assessed and on the fractionation schedule.

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References

ANG, K. K., VAN DER KOGEL, A. J. & VAN DER SCHUEREN, E., 1985. Lack of evidence for increased tolerance of rat spinal cord with decreasing fractioned doses below 2 Gy. *International Journal of Radiation Oncology, Biology, Physics, 11*, 105–110.

BARENDSEN, G. W., 1977. Dose fractionation, dose rate and iso-effect relationships for normal tissue responses. *International Journal of Radiation Oncology, Biology, Physics, 8*, 1981–1996.

DOWN, J. D., 1986. *Comparative Aspects of Radiation Damage to the Rodent Lung*, PhD thesis (University of London).

FIELD, S. B. & HORNSEY, S., 1974. Damage to mouse lung with neutrons and X-rays. *European Journal of Cancer, 10*, 621–627.

FIELD, S. B., HORNSEY, S. & KUTSUTANI, Y., 1976. Effects of fractionated irradiation on mouse lung and a phenomenon of slow repair. *British Journal of Radiology, 49*, 700–707.

FINNEY, D. J., 1964. *Probit Analysis*, 2nd edn (Cambridge University Press, London).

Fisher, D. R. & Hendry, J. H., 1988. Dose fractionation and hepatocyte colonogens: α/β 1–2 Gy, and decreases with increasing delay before assay. *Radiation Research, 113*, 51–57.

Gross, N. J., 1978. Experimental radiation pneumonitis: changes in physiology of the alveolar surface. *Journal of Laboratory Clinical Medicine, 92*, 991–1001.

—— 1981. The pathogenesis of radiation-induced lung damage. *Lung, 159*, 115–125.

Herrmann, Th., Voigtmann, L., Knorr, A., Lorenz, J. & Johanssen, U., 1986. The time–dose relationship for radiation-induced lung damage in pigs. *Radiotherapy and Oncology, 5*, 127–135.

Hopewell, J. W., Barnes, D. W. H., Robbins, M. E. C., Sansom, J. M., Knowles, J. F. & van den Aardweg, G. J. M. J., 1988. The relative biological effectiveness of fractionated doses of fast neutrons (42 MeV$_{d \rightarrow Be}$) for normal tissues in the pig. I. Effects on the epidermis and dermal vascular/connective tissues. *British Journal of Radiology, 61*, 928–938.

Johnson, P. M., Sagerman, R. H. & Dombrowski, C. S., 1970. Ischemia of the lung due to ionizing radiation: quantitative studies. *Journal of Nuclear Medicine, 11*, 491–495.

Law, M. P., Ahier, R. G. & Coultas, P. G., 1986. The role of vascular injury in the radiation response of mouse lung. *British Journal of Cancer, 53*, Supplement VII, 327–329.

Lebesque, J. V., Stewart, F. A. & Hart, A. A. M., 1986. Analysis of rate of expression of radiation-induced renal damage and the effects of hyperfractionation. *Radiotherapy and Oncology, 5*, 147–157.

Mah, K., van Dyck, J., Keane, T. & Poon, P. Y., 1987. Acute radiation-induced pulmonary damage: a clinical study on the response to fractionated radiation therapy. *International Journal of Radiation Oncology, Biology, Physics, 13*, 179–188.

McLaughlin, R. F., Styler, W. S. & Canada, R. O., 1961. A study of the subgross pulmonary anatomy in various mammals. *American Journal of Anatomy, 108, 149–165.*

Moustafa, H. F. & Hopewell, J. W., 1977. Measurement of lung function in the pig after local x-irradiation. In: *Radiobiological Research and Radiotherapy Vol. I* (IAEA, Vienna), pp. 75–83.

Parkins, C. S. & Fowler, J. F., 1985. Repair in mouse lung of multifraction X rays and neutrons: extension to 40 fractions. *British Journal of Radiology, 58*, 1097–1103.

Parkins, C. S., Fowler, J. F., Maughan, R. L. & Roper, M. J., 1985. Repair in mouse lung for up to 20 fractions of X rays or neutrons. *British Journal of Radiology, 58*, 225–241.

Prato, F. S., Kurdyak, R. Saibil, E. A., Carruthers, J. S., Rider, W. D. & Aupin, N., 1976. The incidence of radiation pneumonitis as a result of single fraction upper half body irradiation. *Cancer, 39*, 71–79.

Rezvani, M. & Hopewell, J. W., 1986. The validity of different methods of analysis of Xe-133 washout curves for the determination of lung function. *Nuclear Medicine in Biology, 13*, 245–251.

Rezvani, M., Heryet, J. C. & Hopewell, J. W., 1989. Effects of the single doses of radiation on pig lung. *Radiotherapy and Oncology, 15*, in press.

Thames, H. D., 1985. An "incomplete-repair" model for survival after fractionated and continuous irradiations. *International Journal of Radiation Biology, 47*, 319–339.

Thames, H. D., Withers, H. R. & Peters, L. J., 1984. Tissue repair capacity and repair kinetics deduced from multifractionated or continuous irradiation regimens with incomplete repair. *British Journal of Cancer, 49*, Supplement VI, 263–269.

Travis, E. L. & Down, J. D., 1981. Repair in mouse lung after split doses of X rays. *Radiation Research, 87*, 166–174.

Travis, E. L., Parkins, C. S., Down, J. D., Fowler, J. F. & Thames, H. D., 1983. Repair in mouse lung between multiple small doses of X rays. *Radiation Research, 94*, 326–339.

Travis, E. L. & Tucker, S. L., 1987. Isoeffect models and fractionated radiation therapy. *International Journal of Radiation Oncology, Biology, Physics, 13*, 283–287.

Ts'ao, C.-H., Ward, W. F. & Port, C. D., 1983a. Radiation injury in rat lung. I. Prostacyclin (PG12) production, arterial perfusion and ultrastructure. *Radiation Research, 96*, 284–293.

—— 1983b. Radiation injury in rat lung. III. Plasminogen activator and fibrylonitic inhibitor activities. *Radiation Research, 96*, 301–308.

Tucker, S. L., 1984. Tests for the fit of the linear-quadratic model to radiation isoeffect data. *International Journal of Radiation Oncology, Biology, Physics, 10*, 1933–1939.

Ulrich, R. & Meyer, K. R., 1982. The influence of butylated hydroxytoluene-induced cell proliferation on mouse lung damage after X rays or fission neutrons. *Radiation Research, 89*, 428–432.

van Dyk, J., Keane, T. J., Kan, S., Rider, W. D. & Fryer, C. J. H., 1981. Radiation pneumonitis following large single-dose irradiation based on absolute dose to lung. *International Journal of Radiation Oncology, Biology, Physics, 7*, 461–467.

Wara, W. M., Phillips, T. L., Margolis, L. W. & Smith, V., 1973. Radiation pneumonitis: a new approach to the derivation of time-dose factors. *Cancer, 32*, 547–552.

Ward, W. F., Solliday, N. H., Molteni, A. & Port, C. D., 1983. Radiation injury in rat lung. II. Angiotensin-converting enzyme activity. *Radiation Research, 96*, 294–300.

1990, *The British Journal of Radiology*, *63*, 51–58

Prognostic factors of nasopharyngeal carcinoma: a review of 759 patients

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Abstract. The records of 759 Stage I to IV nasopharyngeal carcinoma patients seen between January 1976 and December 1983 were reviewed. There were 72 (9.5%), 162 (21.3%), 317 (41.8%) and 208 (27.4%) patients with Stage I, II, III and IV disease, respectively. Ho's stage classification was found to give a reliable prognosis. The actuarial survival at 5 and 10 years for Stage I, II, III and IV disease was 80.8%, 71.5%, 40.7%, 17.7% and 33.4%, 48.4%, 30.0%, 9.5%, respectively. The significant factors affecting survival were found using Cox multivariate analysis, N and T stages, the size and degree of fixation of neck nodes, sex, age, the presence of cranial nerve palsy and ear symptoms at presentation. Bilateral neck node involvement, histology subtypes of tumour, headache and nasal symptoms at presentation, the difference in radiation dose to the primary tumour and the neck, the initial haemoglobin and white blood count were not significant factors in the present study. The N stage was found to be prognostically significant even among patient groups stratified for the size and degree of fixation of the neck nodes involved. Women had a better survival rate than men, and the survival of patients less than 40 years old was better than those who were older at 5 years, although by 10 years the survival for the two groups was comparable.

Among head and neck tumours, nasopharyngeal carcinoma (NPC) is a special entity in that its location does not lend itself to curative surgery, and radiotherapy is the primary treatment. Nasopharyngeal carcinoma is also peculiar in that no single stage classification for it has been widely accepted. The International Union against Cancer (UICC) and American Joint Committee on Cancer (AJC) staging systems, although widely adopted for other head and neck cancers, have not been uniformly accepted for NPC (Fu, 1980). One reason for this lack of support for NPC staging with these systems is that they were basically designed for surgical management, while the definitive treatment of NPC is radiotherapy (Ho, 1978). Nasopharyngeal carcinoma is a common cancer in our part of the world and for a number of years we have used Ho's stage classification and found it useful. It is unfortunate that Ho's stage classification has not been more widely employed. Here, we review our experience of this disease, Ho's stage classification and other factors that affected the treatment results.

Patients and methods

From January 1976 to December 1983, 841 patients with newly diagnosed nasopharyngeal carcinoma were referred to our department. Forty-five patients either refused treatment or died from advanced disease before the completion of radiotherapy and were excluded from the present analysis. Another 37 patients had distant metastasis (Stage V disease) and were not given radical treatment. The actuarial survival data of these patients were computed for comparison with other stages, but their data were not used in the analysis for factors affecting survival. The remaining 759 Stage I to IV patients formed the basis of the present analysis.

There were 561 male and 198 female patients. Their age ranged from 15 to 83 years with a median age of 49 (Table I). All patients had histological confirmation by biopsy of the primary tumour in the nasopharynx; 427 (56.3%) of the tumours were classified as undifferentiated carcinoma, 283 (37.3%) as poorly differentiated squamous carcinoma, 31 (4.0%) were not subclassified and 16 (2.1%) and two (0.3%) were classified as moderately and well differentiated squamous carcinoma respectively.

A history was taken at the initial consultation with special emphasis on nasal symptoms (such as epistaxis, nasal discharge), headache and ear symptoms (such as tinnitus, deafness) from all patients. All patients were then examined for cervical lymphadenopathy. The position of the nodes in relation to the three levels of the neck, the dimension of the nodes and the degree of fixation were noted and documented by line drawings. In addition to general examination, special care was

Table I. Age distribution

Age	Number of patients	%
<20	6	0.8
20–29	39	5.1
30–39	150	19.8
40–49	195	25.7
50–59	221	29.1
60–69	121	15.9
70 and above	27	3.6

Median age = 49 years.

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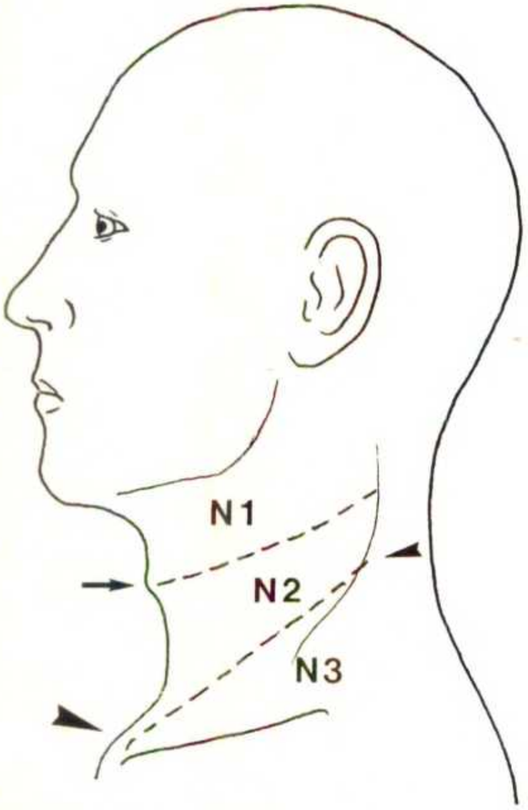


Figure 1. The three regions of neck for N stage classification. The first and second regions were divided by the skin crease extending from the laryngeal eminence (arrow) laterally; the second and third regions were divided by the line joining the upper margin of the sternal end of the clavicle (large arrow head) and the apex of an angle formed by the lateral surface of the neck and the superior margin of of the trapezius (small arrow head).

Table II. Stage classification (Ho, 1970)

Primary tumour

- T_1 Those tumours confined to the nasopharynx
- T_2 Those tumours which had extended to the nasal fossa, oropharynx, or adjacent muscles and nerves below the base of skull
- T_3 Those tumours which had extended beyond the T_2 limit (including those with erosion of the base of skull, cranial nerve palsy)

Neck node

The neck is divided into three regions by the skin crease extending from the laryngeal eminence laterally, and the line joining the upper margin of the sternal end of the clavicle and the apex of an angle formed by the lateral surface of the neck and the superior margin of the trapezius (Fig. 1).

- N_0 No clinically palpable neck node
- N_1 Nodes entirely inside the uppermost region of neck
- N_2 When the lowest lying node had involved the middle region of the neck
- N_3 When the lowest lying node had involved the most inferior region of the neck

Distant metastasis

- M_0 No evidence of distant metastasis
- M_1 Any distant metastasis

Stage grouping

	T_1	T_2	T_3
N_0	I		
N_1		II	
N_2			III
N_3		IV	
	M1	V	

taken to identify oropharyngeal and nasal extension of the disease and cranial nerve palsies. Clinical examination was complemented by chest radiograph, liver function test and the standard five views of the nasopharynx, which are particularly useful for the detection of tumour invasion of the base of skull (Ho, 1967).

All patients were staged according to Ho's stage classification system as shown in Table II and Fig. 1 (Ho, 1970). Bilateral nodal involvement does not influence the N stage. In addition to the usual staging, patients with cervical lymphadenopathy were grouped into three types according to the size and degree of fixation of the nodes: Type 1 consisted of patients with mobile nodes less than 4 cm in diameter, Type 2 consisted of patients with nodes between 4 cm and 6 cm, or partially fixed nodes. Type 3 patients had nodes of at least 6 cm or fixed nodes.

Six hundred and sixty-nine patients were treated by cobalt 60 or linear accelerator using the techniques as described by Ho (1982); 290 (38.2%) of them were treated by split-field technique with two lateral opposing facial fields and one anterior facial field for the primary tumour. A central tumour dose of 3.5 Gy or 3.8 Gy per fraction was given three times a week aiming at a total of 53.2 Gy to 59.5 Gy, while the neck was treated concurrently with matching anterior cervical field. Three hundred and seventy-nine patients (49.9%) were treated by lateral opposing facio-cervical fields for the initial phase of treatment; a midplane tumour dose of 2.5 Gy per fraction was given four times a week to 40 Gy, while the neck was treated concurrently with matching lower anterior cervical field. Phase two treatment was given by split-field technique with two lateral opposing facial fields and one anterior facial field and a central tumour dose of 3.5 Gy or 3.8 Gy per fraction was given three times a week aiming at another 14 Gy to 21 Gy.

Ninety patients (11.9%) were treated with an orthovoltage machine with two anterior oblique and two posterior oblique fields; 1.5 Gy was given daily to 30 Gy. This was followed by 3.5–3.8 Gy per fraction given three times a week aiming towards another 30.4–31.5 Gy.

Table III. T and N stage distribution

	T_1	T_2	T_3	Total number of patients
N_0	72	5	49	126
N_1	149	8	60	217
N_2	153	13	42	208
N_3	123	29	56	208
Total number of patients	497	55	207	

Table IV. N stage distribution for patients with unilateral and bilateral neck node involvement

	N_1	N_2	N_3
Unilateral nodal involvement	176 (49.0%)	116 (32.3%)	67 (18.7%)
Bilateral nodal involvement	41 (15.0%)	92 (33.6%)	141 (51.4%)

$p < 0.0001$.

Most of these patients were treated in the earlier period and had bulky neck node involvement.

Concurrent neck treatment was given to all patients, either as matching anterior cervical field for the technique with three facial fields or as matching lower anterior cervical field for the technique with lateral opposing facio-cervical fields. The radiation was given either as therapy for neck node metastasis or as prophylaxis for those with no clinically palpable nodes. The technique and dose was the same for both groups of patients: both sides of neck were treated from the level of the mastoid to just above the supraclavicular fossae, aiming for a dose ranging from 45.6 Gy/12 fractions/4 weeks to 54 Gy/20 fractions/5.5 weeks.

After completion of radiotherapy, all patients were followed up every 4 to 6 weeks during the first year, then every two months during the second year and every three months during the third year. The time interval between follow-ups was then gradually increased to every half-year, and follow-ups were continued indefinitely. At each visit, the nasopharynx, the neck and the abdomen were carefully examined. Chest radiography was performed yearly. Other radiological and blood tests were done when clinical symptoms and signs indicated the need.

The median follow-up duration for the whole group of patients was 64 months, the maximum being 149 months. Forty-four patients were lost from the follow-up, 26 of whom had been followed up for more than 2 years.

The factors affecting survival were determined by survival analysis with covariates using Cox's models (Cox, 1972). The actuarial survival rate for patients were stratified for N stage, T stage, node characteristics, laterality of neck node involvement, sex, age and the presence or absence of ear symptoms and cranial nerve palsies at presentation; these were computed by the Kaplan–Meier method and the difference between curves tested by the Mantel–Cox test (Kaplan & Meier, 1958; Mantel & Haenszel, 1959). Computations were performed by the 1L and 2L modules of the BMDP Statistical Software.

Results

The age distribution of these 759 patients is shown in Table I. The T and N stage distribution of patients are shown in Table III. There was no linear correlation between the T stage and the N stage ($p = 0.22$). The stage grouping of these patients was 72 (9.5%) with Stage I disease, 162 (21.3%) with Stage II, 317 (41.8%) with Stage III and 208 (27.4%) with Stage IV.

Among patients with neck node metastasis, 359 (56.7%) had unilateral and 274 (43.3%) had bilateral node involvement. Patients with bilateral node involvement tended to have more advanced N stage status. The N_1, N_2, and N_3 distribution was 176 (49.0%), 116 (32.3%) and 67 (18.7%) respectively for the group with unilateral node involvement; 41 (15.0%), 92 (33.6%) and 141 (51.4%) respectively for the group with bilateral node involvement (Table IV). The difference in N stage distribution between the two groups was statistically significant ($p < 0.0001$ by χ^2-test).

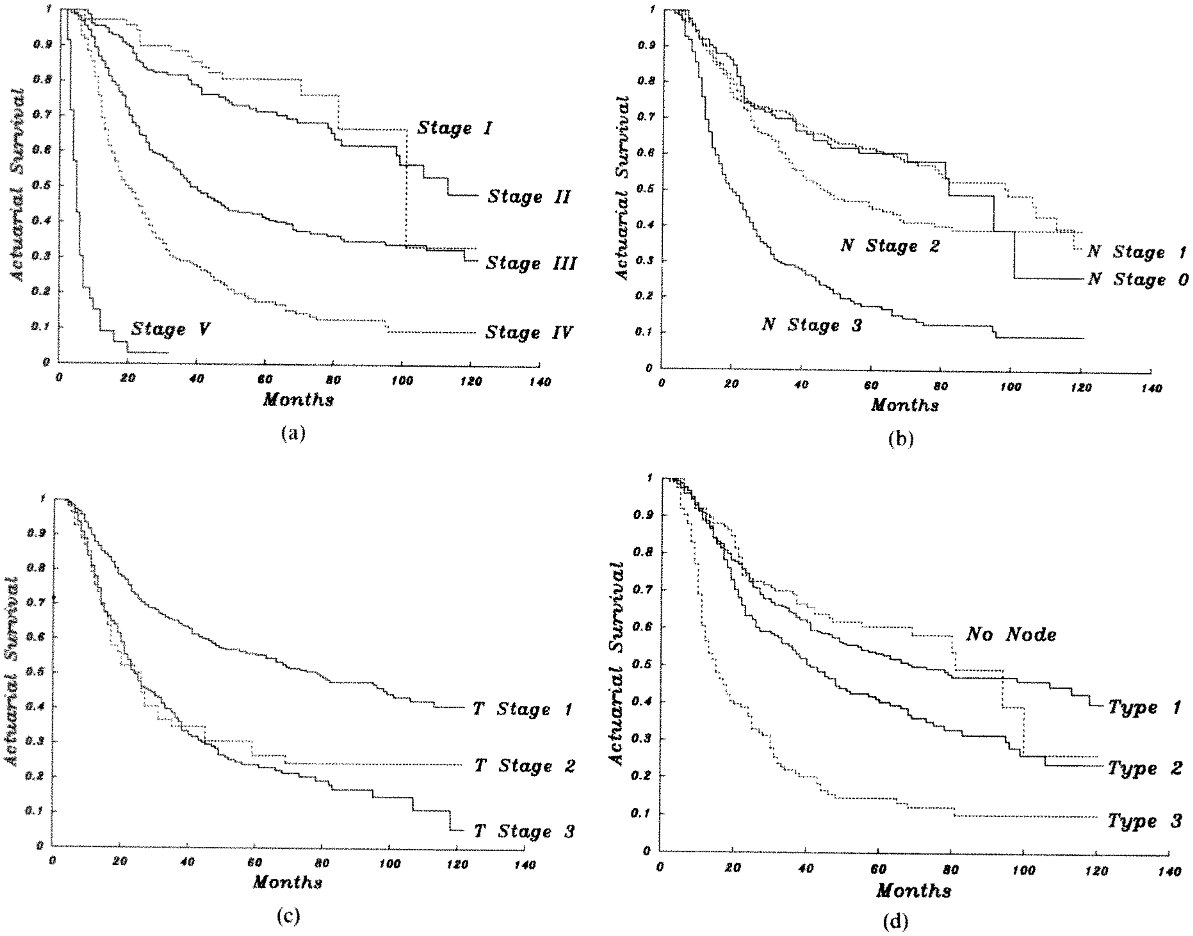
Among the patients with neck node involvement, there were 310 (49.0%) with Type 1, 200 (31.6%) with Type 2, and 123 (19.4%) with Type 3 involvement.

The stage distribution between male and female patients, patients below 40 years of age and those above

Table V. Stage distibution by sex and age

	Stage I	Stage II	Stage III	Stage IV
Sex[a]				
Male	52 (9.3%)	109 (19.4%)	238 (42.4%)	162 (28.9%)
Female	20 (10.1%)	53 (26.8%)	79 (39.9%)	46 (23.2%)
Age[b]				
less than 40 years of age	31 (15.9%)	60 (30.8%)	53 (27.2%)	51 (26.1%)
40 years and above	95 (16.8%)	157 (27.8%)	155 (27.5%)	157 (27.8%)

[a] $p = 0.13$.
[b] $p = 0.88$.



(a) (b) (c) (d)

Figure 2. Actuarial survival by (a) Stage, (b) N stage, (c) T stage, (d) node characteristics ($p<0.0001$).

are shown in Table V. There was no significant difference in the stage distribution between different sex and age groups ($p=0.13$ and 0.88 respectively, by χ^2-test).

One hundred and forty (18.4%) patients relapsed locally in the nasopharynx, 162 (21.3%) patients relapsed regionally in neck node and 183 patients (24.1%) developed distant metastasis.

The N stage, T stage, node characteristics (type of involvement), sex, age, the presence of cranial nerve palsy and ear symptoms at presentation were found to be significant factors affecting the survival, using Cox multivariate analysis. Bilateral neck node involvement, histology subtypes of tumour, headache and nasal symptoms at presentation, the difference in radiation dose to the primary tumour and the neck and the initial haemoglobin and white blood count were not significant factors affecting survival in the present study.

The actuarial survival of patients with N stage, T stage and the types of neck node involvement are plotted in Fig. 2. The difference between curves in each group was significant ($p<0.0001$ in all four).

The N stage classification remained prognostically discriminating in patient groups stratified for type of node involvement (Fig. 3, $p<0.0001$, $p<0.0001$ and $p=0.063$ respectively).

For patients with N_1 disease, bilateral nodal involvement adversely affected the survival (Fig. 4a, $p=0.023$). For patients with N_2 or N_3 disease, those with unilateral involvement had slightly better survival than those with bilateral involvement, but the difference was not statistically significant (Fig. 4b, $p=0.26$ and 0.16 respectively).

The actuarial survival of patients of different sex is plotted in Fig. 5a. Female patients had better survival ($p=0.0001$) among patients with Stage II and III disease ($p=0.0016$ and 0.0059 respectively), but was not discernable in patients with Stage I and IV disease ($p=0.45$ and 0.84 respectively).

The actuarial survival of patients below the age of 40 and above 40 is plotted in Fig. 5b. The difference between the survival pattern of the two groups of patients was significant ($p=0.0021$). The survival was better in the earlier years for patients less than 40 years

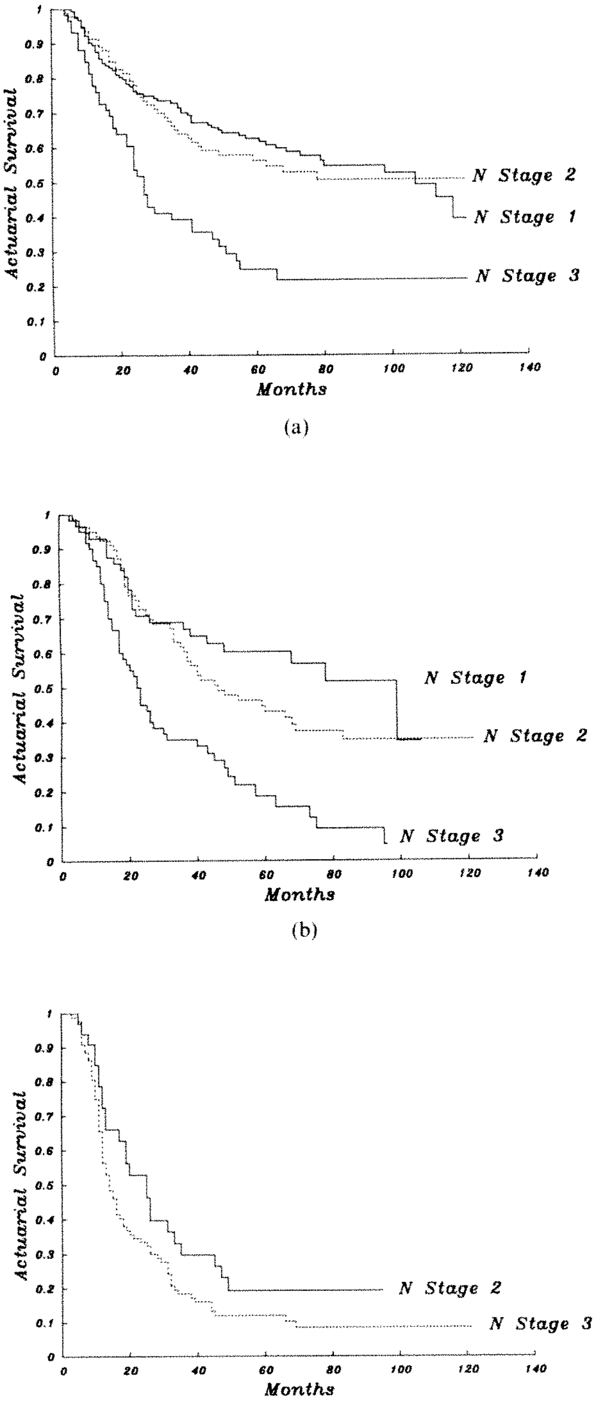


Figure 3. Actuarial survival by N stage for patients (a) with mobile nodes less than 4 cm in diameter (Type 1 node involvement) ($p<0.0001$), (b) with nodes between 4 cm and 6 cm or partially fixed (Type 2 node involvement) ($p<0.0001$), (c) with nodes 6 cm or larger or fixed (Type 3 node involvement) ($p=0.063$).

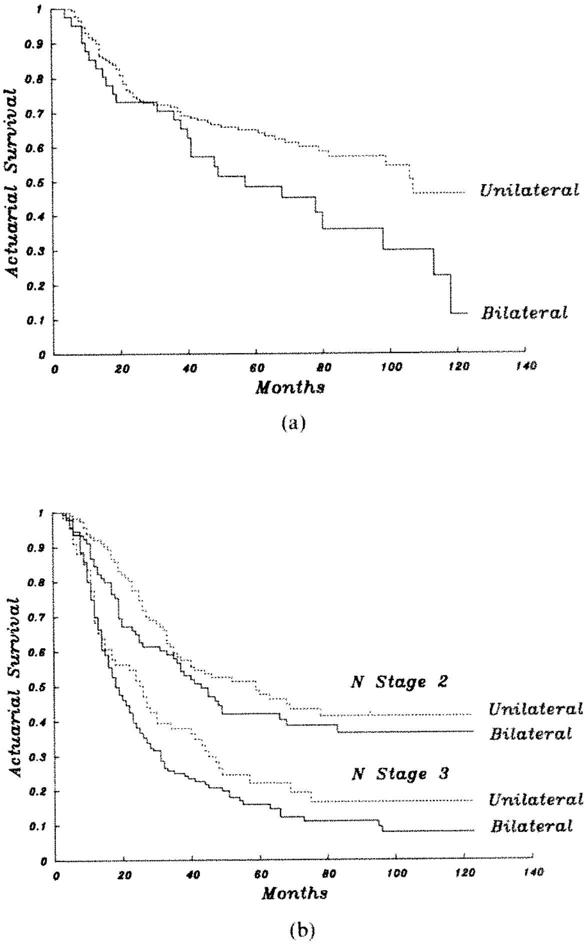
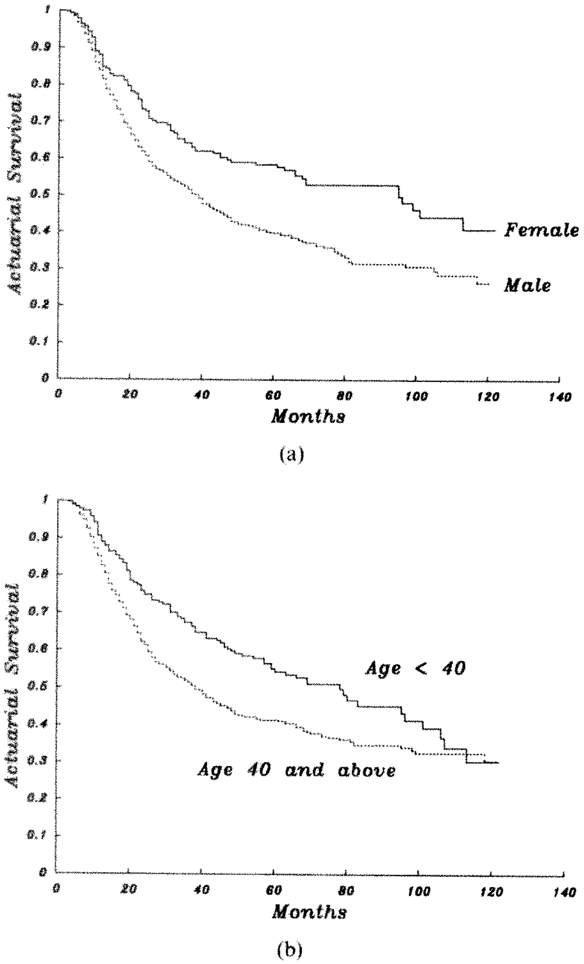


Figure 4. Actuarial survival of (a) N_1 ($p=0.023$) and (b) N_2 ($p=0.26$) and N_3 ($p=0.16$) patients with unilateral or bilateral nodal involvement.

of age, but after the fifth year, their survival tended to catch up with the older patients: by the ninth year their survival became comparable. When analysed after stratification for stage, the same pattern occurred for Stage I, II and III patients, even though the difference was not statistically significant for Stage II patients ($p=0.02$, 0.25, and 0.02 respectively). This pattern was not discernable for patients with Stage IV disease ($p=0.90$).

The presence of ear symptoms was an adverse prognostic factor in patients with T_1 disease (Fig. 6a, $p=0.018$), but was not significant in patients with T_2 and T_3 disease ($p=0.75$ and 0.33, respectively).

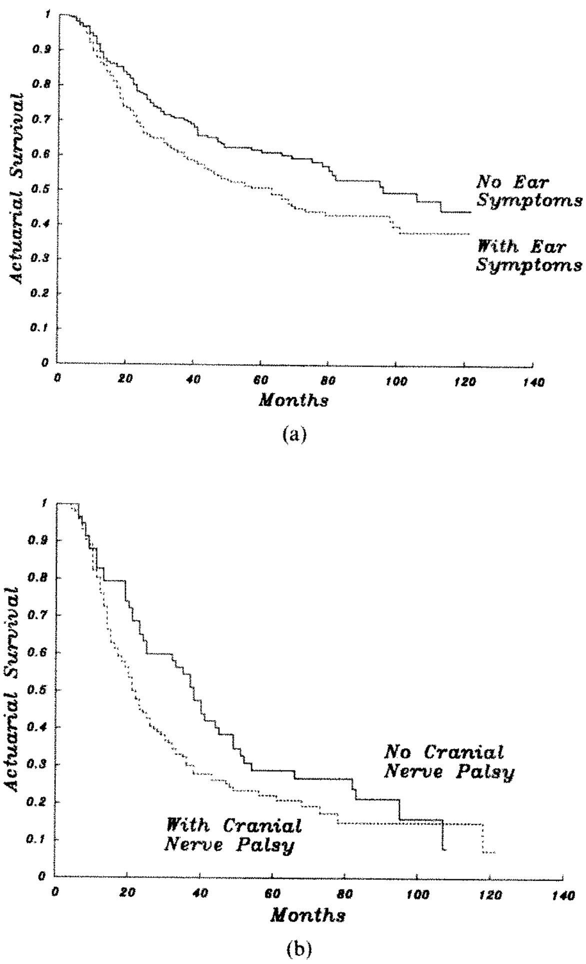
The presence of cranial nerve palsy with or without associated radiological evidence of base of skull erosion tended to adversely affect the survival of the T_3 patients, when compared with patients staged as T_3 by radiological evidence of base of skull erosion only (Fig. 6b, $p=0.063$).



(a)

(b)

Figure 5. Actuarial survival by (a) sex ($p = 0.0001$) and (b) age ($p = 0.0021$).



(a)

(b)

Figure 6. Actuarial survival of (a) T_1 patients, with or without ear symptoms ($p = 0.018$), and (b) T_3 patients, with or without cranial nerve palsy ($p = 0.063$).

There were some complications: all patients had a dry month of various degrees; 68 (9.0%) patients developed neck fibrosis and 41 (5.4%) patients developed late central nervous system complications at one or more sites: four of these (0.5%) suffered from temporal lobe damage, three (0.4%) had myelopathy with long tract signs and 36 (4.7%) had cranial nerve palsy. The cranial nerves involved in isolation or combined with others were the twelfth in 27 patients, the eleventh in six patients, the sixth in six patients, the second in four patients, and the tenth in two patients. There were six patients with endocrine dysfunctions showing hyperprolactinaemia, hypogonadism, and hypothyroidism.

Discussion

Our study confirmed the validity of Ho's stage classification, which separated patients into distinct prognostic groups. Although there was overlap in the survival curves of Stage I and II patients after the eighth year (Fig. 2a), this can be explained by chance because the number of patients with Stage I disease still under observation at that time was small. The individual components of the stage classification, *i.e.*, the T stage and N stage, were predictive; the T staging system, however, needs refinement in that the prognostic significance of T_2 and T_3 staging were comparable.

Evidence from reported series support the division of T stage between the group with tumour extension below the base of skull (T_2), and T_3 disease with erosion of the base of the skull or cranial nerve palsies (Hoppe et al, 1976; Huang, 1980; Mesic et al, 1981), although Qin et al (1988) did not rank the significance of involvement of these two groups of structures, but considered the number of these groups of structures being involved as important. The lack of difference between T_2 and T_3 diseases in our series probably reflected the inadequacy of clinical examination and plane radiographs without the use of computed tomography (CT) in detecting parapharyngeal, nasal and oropharyngeal extension of the tumour (Yu et al, 1985). The tumour with clinically evident extension to these sites can be more extensive than a tumour with early invasion of the cavernous sinus and impinged on the sixth cranial nerve.

The inadequacy of clinical examination and plane radiographs without the use of CT as a T staging procedure was highlighted in the adverse effect of ear symptoms in our patients with T_1 disease. What was seen in the nasopharynx might only be a small part of the tumour. The soft-tissue components of the superior and lateral extension of tumour could not be detected by plane radiographs until it reached a bony structure and eroded it. But such extension could appear in some patients as ear symptoms resulting from mechanical or functional derangement of the Eustachian tube.

In concordance with reported experience (Huang, 1980; Neel at al, 1985), the present study also confirmed the adverse prognostic effect of cranial nerve palsy among patients with T_3 disease. This will be another point for the "fine-tuning" of the T stage system.

There is also room for improvement in the N staging system. The survival of patients with N_0 and N_1 disease was comparable, and patients with N_0 disease had worse survival after the seventh year (Fig. 2b). This highlights the fact that the first station node of nasopharyngeal carcinoma lies in the retropharyngeal space, those clinically palpable nodes in the upper neck are at least the second stations (Neel et al, 1985). This has important implications for treatment. The biological difference between a tumour with involvement of the retropharyngeal nodes alone and another which has also spread to nodes clinically palpable in the upper neck may be small. What may be more important is that the presence of clinically palpable cervical nodes draws the attention of the clinician of the need to deal with it. The involvement of the retropharyngeal nodes without further extension to clinically palpable cervical chain may easily result in marginal miss; the use of CT in the staging procedures of nasopharyngeal carcinoma may result in improvement in this respect (Yu et al, 1985).

Although the N stage is discriminating even in patient groups stratified for the characteristics of neck nodes involved, the characteristics of the neck nodes involved was a prognostic factor independent of the N stage, which may be refined by incorporating the size and degree of fixation of nodes.

In concordance with Ho (1978) and Neel et al (1985), but contrary to Wang and Meyer (1971), Meyer and Wang (1971), Moench et al (1972) and Hoppe et al (1976), we found bilateral neck node involvement not to be an independent prognostic factor. Bilateral neck node involvement was prognostically significant only in the subgroup of patients with N_1 disease (Fig. 4a). Moench and Phillips (1972) considered contralateral node involvement as N_3, and Wang and Meyer (1971), Meyer and Wang (1971) and Hoppe et al (1976) considered contralateral node involvement as N_2. Fixation of nodes was considered as N_2 and N_3, respectively, by these groups.

The AJC and UICC stage classifications systems consider contralateral node involvement as N_2 and ignore fixation of nodes. The level of neck node involvement was not taken into consideration by any of these groups. We have confirmed the superiority of N staging (by the level of node involvement) over the laterality of nodal involvement. We have also found that bilateral nodal involvement was associated with more advanced N stage (Table IV), which might have indirectly influenced the prognosis. This may explain the difference in prognostic significance of bilaterality of neck node disease in the present and their series.

Ho (1978), Huang (1980) and Qin et al (1988) reported a better 5-year survival of young patients. The present series documented similar results, but in addition, we found that the difference between the survival curves started to diminish after the fifth year, and the survival of the young patients tended to catch up with the older patients at the ninth year. A similar pattern prevailed in subgroups of patients stratified for stages. The mechanism of the inferior survival associated with age is an interesting phenomenon that merits further study.

Contrary to the finds of Ho (1978), but in agreement with Meyer and Wang (1971), Huang (1980), Neel et al (1985) and Qin et al (1988), we have been able to confirm the significance of sex on survival. We have also been able to show that such difference remains true after stratification by stage (for Stage II and III patients).

In summary, the present study confirmed the validity of Ho's stage classification and identified possible directions for improvement, *e.g.*, the use of CT to supplement clinical and other radiological examinations in order to discriminate between T_2 and T_3 diseases, to make good the paradoxical reversal of prognosis between N_0 and N_1 disease and the refinement of N staging by incorporating factors of node size and fixation.

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References

AMERICAN JOINT COMMITTEE ON CANCER, 1988. *Manual for Staging of Cancer* (J.B. Lippincott, Philadelphia).

COX, D. R., 1972. Regression models and life tables. *Journal of Royal Statistics Society, Series B, 34*, 187–220.

FU, K. K., 1980. Prognostic factors of carcinoma of the nasopharynx. *International Journal of Radiation Oncology, Biology, Physics, 6*, 523–526.

HO, J. H. C., 1967. Radiological Diagnosis of nasopharyngeal carcinoma with special reference to its spread through the base of skull. In *Nasopharyngeal Cancer UICC Monograph Series*, Vol. I, ed. by C.S. Muir and K. Shanmugaratnam (Medical Examination Publishing Company Ltd., New York), pp. 238–246.

——1970. The natural history and treatment of nasopharyngeal carcinoma. In *Oncology* (Proceedings of the 10th International Cancer Congress), Vol. 4, ed. by R. Lee-Clark, R. W. Cumley, J. E. McKay and M. Copeland (Year Book, Chicago), pp. 1–14.

——1978. An epidemiologic and clinical study of nasopharyngeal carcinoma. *International Journal of Radiation Oncology, Biology, Physics, 4*, 183–198.

——1982. Nasopharynx. In *Treatment of Cancer*, ed. by K. E. Halnan (Chapman and Hall, London), pp. 249–267.

HOPPE, R. T., GOFFINET, D. R. & BAGSHAW, M. A., 1976. Carcinoma of the nasopharynx, eighteen years' experience with megavoltage radiation therapy. *Cancer, 37*, 2605–2612.

HUANG, S. C., 1980. Nasopharyngeal cancer: a review of 1605 patients treated radically with cobalt 60. *International Journal of Radiation Oncology, Biology, Physics, 6*, 401–407.

INTERNATIONAL UNION AGAINST CANCER, 1987. *TNM Classification of Malignant Tumours* (Springer-Verlag, Berlin).

KAPLAN, E. L. & MEIER, P., 1958. Non-parametric estimation from incomplete observations. *Journal of American Statistics Association, 53*, 457–481.

MANTEL, N. & HAENSZEL, W., 1959. Statistical aspects of the analysis of data from retrospective studies of disease. *Journal of National Cancer Institute, 22*, 719–748.

MESIC, J. B., FLETCHER, G. H. & GOEPFERT, H., 1981. Megavoltage irradiation of epithelial tumors of the nasopharynx. *International Journal of Radiation Oncology, Biology, Physics, 7*, 447–453.

MEYER, J. E. & WANG, C. C., 1971. Carcinoma of the nasopharynx, factors influencing results of therapy. *Radiology, 100*, 385–388.

MOENCH, H. C. & PHILLIPS, T. L., 1972. Carcinoma of the nasopharynx, review of 146 patients with emphasis on radiation dose and time factor. *American Journal of Surgery, 124*, 515–518.

NEEL, H. B., TAYLOR, W. F. & PEARSON, G. R., 1985. Prognostic determinants and a new view of staging for patients with nasopharyngeal carcinoma. *Annual of Otology, Rhinology, Laryngology, 94*, 529–537.

QIN, D., HU, Y., YAN, J., XU, G., CAI, W., WU, X., CAO, D. & GU, X., 1988. Analysis of 1379 patients with nasopharyngeal carcinoma treated by radiation. *Cancer, 61*, 1117–1124.

WANG, C. C. & MEYER, J. E., 1971. Radiotherapeutic management of carcinoma of the nasopharynx, an analysis of 170 patients. *Cancer, 28*, 566–570.

YU, Z. H., XU, G. Z., HUANG, Y. R., HU, Y. H., SU, X. G. & GU, X. Z., 1985. Value of computed tomography in staging the primary lesion (T staging) of nasopharyngeal carcinoma (NPC): an analysis of 54 patients with special reference to the parapharyngeal space. *International Journal of Radiation Oncology, Biology, Physics, 11*, 2143–2147.

1990, *The British Journal of Radiology*, *63*, 59–64

A method for the assessment of the output of irregularly shaped electron fields

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Abstract. A simple approach to the calculation of dose in cone-collimated electron fields is presented. The method accounts for variations in lateral scatter with field size using a Clarkson Integration. The reduction in output by an irregularly shaped aperture is evaluated based on measurements of the output at various distances from the aperture in a field 2.5 cm in diameter. The first 14 months of clinical use were analysed and it is shown that in 42 out of 600 calculations, the cutout factor was less than 0.95 and that in 77% of these, the calculation method was accurate to ±3%.

Manufacturers of radiotherapy linear accelerators have provided simple means to construct apertures to define irregularly shaped electron fields. In our experience, with a Clinac-18 and 1800 (Varian Associates), this results in all electron fields being shaped for the individual patient. The output of these cones is reduced by the insertion of an aperture as a result of the loss of scatter in the patient and scatter from the cone, by as much as 25%.

There have been reports on the use of pencil-beam algorithms to predict the dose in irregularly shaped electron fields (Kooy & Rashid, 1980; Bruinvis et al, 1983; McParland, 1989). The related concept of lateral build-up factor has been applied to this problem (Kahn et al, 1987). Dutreix and Briot (1985) describe a method of calculation similar to that used for photon beams, in which the scatter in sectors is summed following the method of Clarkson. The use of experimentally determined factors and relationships between the open field and the irregular field have been used by other workers (Biggs et al, 1979; Sharma et al, 1984; Mills et al, 1985).

We have developed a computer program, "CUTOUT", which calculates the monitor unit setting required to deliver the prescribed dose. The program has been in use since the beginning of 1987, and we report an analysis of the first 14 months of operation, when around 600 calculations were made. The program accommodates the wide range of situations encountered in clinical practice such as the use of bolus, extended source–skin distance (SSD) and irregular field shape. The accuracy of the calculation was assessed by measurements on a particular aperture and verification of the dose rate on a wide variety of apertures in clinical use. To some extent, we view the use of this program as a sorting mechanism to identify unusual apertures or set-ups that require more extensive evaluation and have set criteria to identify these, which are discussed below. It should be emphasized that the program is used to calculate the machine setting required to deliver the prescribed dose at a single point.

Methods and materials

We have adopted a similar approach to the calculation of dose in photon fields, in which the primary dose and scatter are calculated separately. The primary dose in this situation may be thought of as the fluence arising directly from the vacuum window, applicator or cone scatter and frame scatter as described by Bruinvis et al (1983). The scatter dose is simply the dose resulting from scatter in the patient which has been shown by many workers to saturate rapidly with field size.

Part of the database we define on a linear accelerator is electron depth-dose determined with a parallel plate ionization chamber in lucite (PMMA) phantom. The procedures outlined by the AAPM (1983) are used to convert the ionization measurements to dose, and Fig. 1 is a typical plot of such depth-dose data. A reference depth is established which is close to dose maximum for the range of field sizes used clinically. Tissue–phantom ratios (TPR) are calculated from the depth-dose data, based on a virtual source location, determined by correlating ionization at the reference depth at various distances from each cone to inverse square law. We assume that the TPRs are the same for a square field and circular field inscribed in the square. Furthermore, we assume that the depth-dose variation is linear with depth for a very small field defined by a line connecting the surface dose of the smallest measured field and the practical range, shown as a dotted line in Fig. 1. The program does not allow the point of calculation to be outside the field. The average TPR is determined by averaging the TPR of fields corresponding to 36 radii taken at 10° intervals around the field perimeter:

$$\overline{\mathrm{TPR}_d} = \frac{1}{36}\sum_{i=1}^{36} (\mathrm{TPR})_d^{r_i} \qquad (1)$$

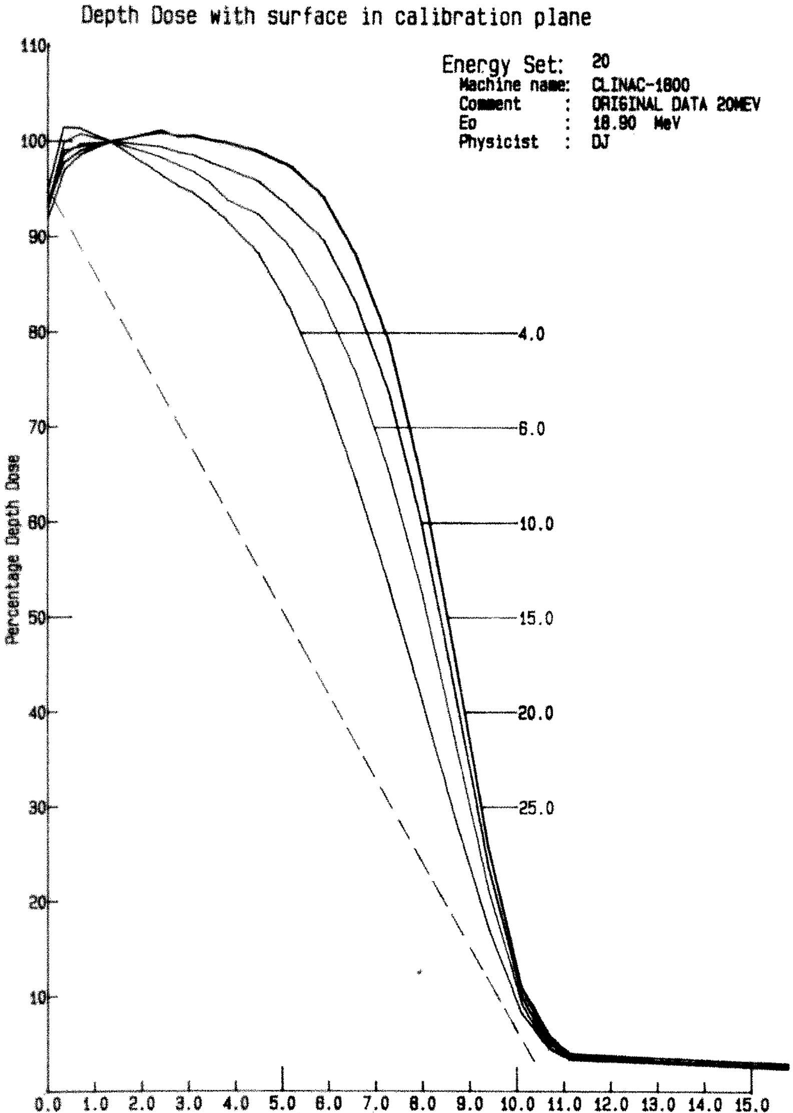


Figure 1. The depth-dose characteristics of a nominal 20 MeV electron beam, showing the variation with cone size.

where d is the depth of the prescription point and r_i is the length of the ith radius.

The calculation of primary dose is based upon measurements with an arrangement illustrated in Fig. 2. A plate with an aperture, 2.5 cm in diameter, centred in each cone is constructed using the same technique as for clinical cutouts. The parallel plate ion chamber (PTW Electron Beam Chamber) is located at a shallow depth in the lucite phantom and the front face of the ion chamber is brought to four positions, namely the isocentre, 3 cm above the isocentre towards the cone and 5 and 10 cm below it. The response of the ion chamber is measured with and without the 2.5 cm aperture plate installed and the ratio of the ionization is referred to as the circular cutout factor. The depth of measurement is not critical; we have shown the circular cutout factors vary less than ±2%, if these measurements are made anywhere in the range 3–12 mm depth. However, the results when there is no cover on the ion chamber, which has a 2.7 mg/cm^2 window, were about 3% lower than the measurements made at depth. Typical results are shown in Fig. 3. The series of measurements made with the open cone are used to establish the virtual source distance from the isocentre. The output (D_o) for the cone is determined with the ion chamber located at the isocentre, with a cover corresponding to the reference depth used for TPR measurements. The nominal SSD when the skin is at the isocentre is 100 cm on the Clinac machines, and the aperture plate is 5 cm away from the isocentre.

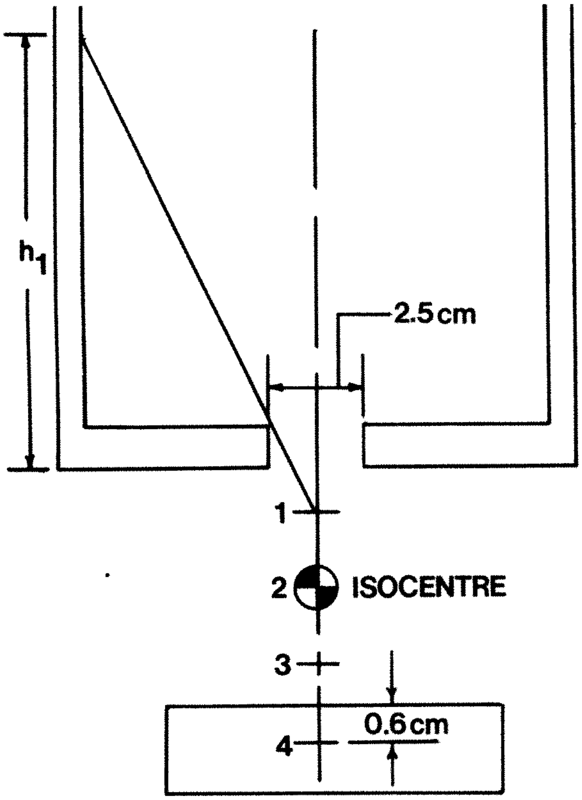


Figure 2. The arrangement used to assess cutout factors.

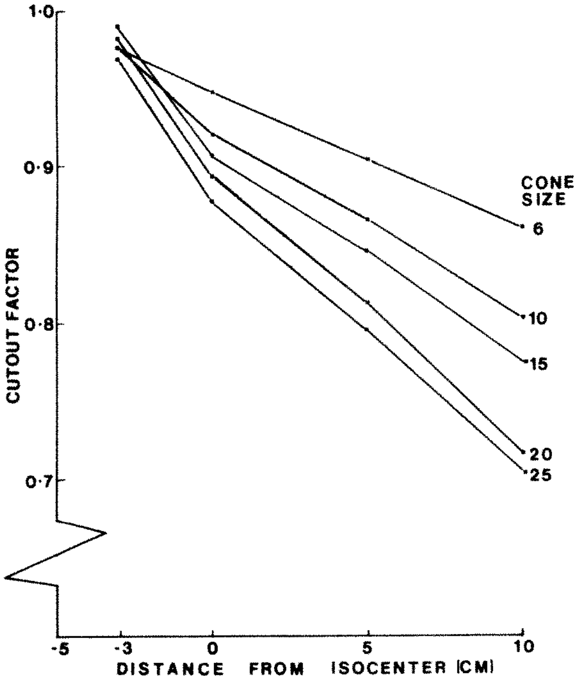


Figure 3. The cutout factors for a 2.5 cm diameter aperture at various distances along the central axis of a 9 MeV electron beam.

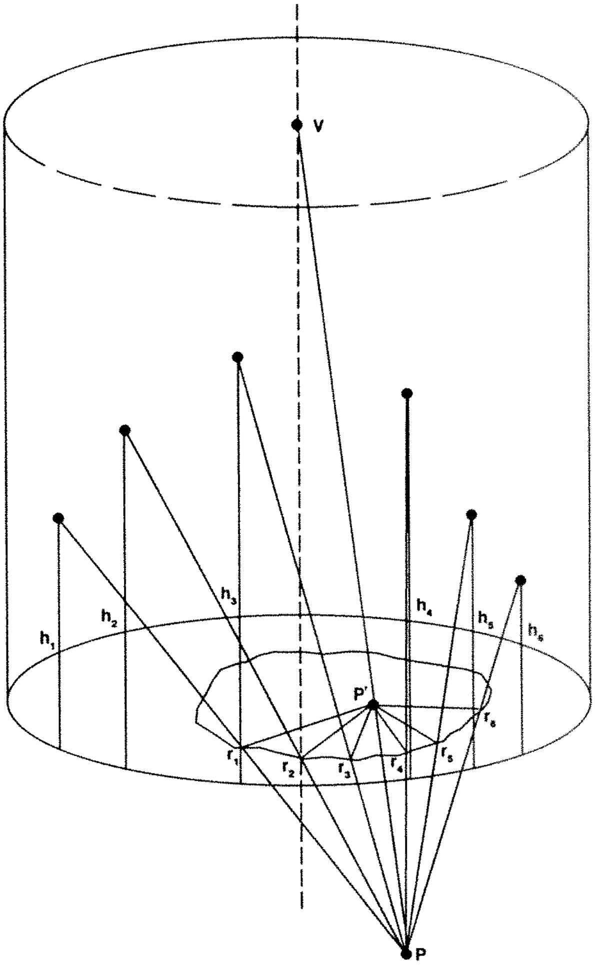
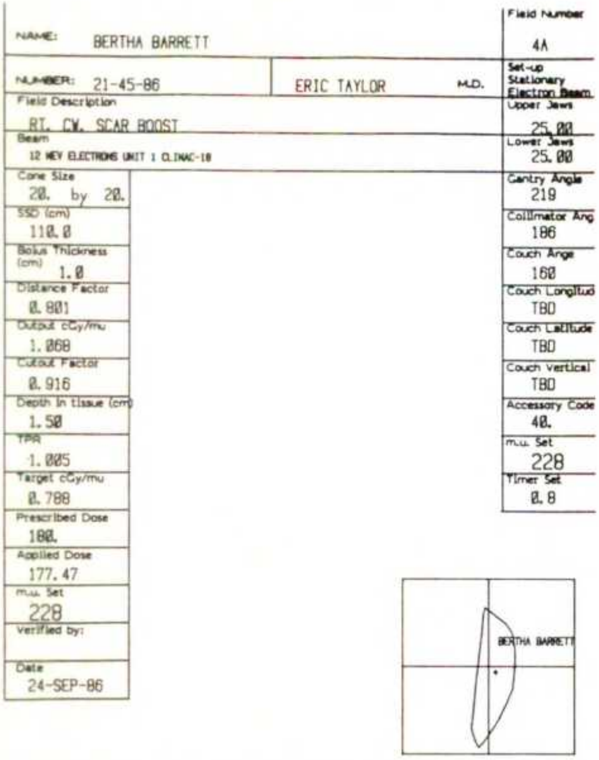


Figure 4. An illustration of the model used for average cutout factor determination.

In Fig. 2 we show a line that passes from the first measurement point through the aperture to strike the inside of the cone at a distance h_1 above the aperture. For the purpose of this model, a cylindrical geometry is assumed and the diameter of the cone is assumed to be the size of the cone. The manufacturer provides cones giving square fields of side 6, 10, 15, 20 and 25 cm. Thus, for a particular cone at a particular energy, we develop a table of cutout factors as a function of distance inside the cone (h). The cutout factor of an irregular aperture is determined by adding 10° increments around the perimeter of an irregular aperture and determining the cutout factor corresponding to the inside height, h, as illustrated in Fig. 4, *i.e.*,

$$\overline{\mathrm{CF}} = \frac{1}{36}\sum_{i=1}^{36} (\mathrm{CF})_{h_i} \qquad (2)$$

where CF = cutout factor. Thus given an SSD, a treatment depth t, bolus thickness b and virtual source



NAME: BERTHA BARRETT

Field Number: 4A

NUMBER: 21-45-86

ERIC TAYLOR M.D.

Set-up: Stationary Electron Beam

Field Description: RT. CW. SCAR BOOST

Upper Jaws: 25.00

Beam: 12 MEV ELECTRONS UNIT 1 CLINAC-18

Lower Jaws: 25.00

Cone Size: 20. by 20.

Gantry Angle: 219

SSD (cm): 110.0

Collimator Ang: 186

Bolus Thickness (cm): 1.0

Couch Ange: 160

Distance Factor: 0.801

Couch Longitud: TBD

Output cGy/mu: 1.068

Couch Latitude: TBD

Cutout Factor: 0.916

Couch Vertical: TBD

Depth in tissue (cm): 1.50

Accessory Code: 40.

TPR: 1.005

m.u. Set: 228

Target cGy/mu: 0.788

Timer Set: 0.8

Prescribed Dose: 100.

Applied Dose: 177.47

m.u. Set: 228

Verified by:

Date: 24-SEP-86

Figure 5. The program's output is plotted, in colour, onto a piece of cardboard and serves as documentation of the layout of the field.

distance V from the isocenter, the output (cGy/mu) at the prescription point P in an irregularly shaped field is given by:

$$D_p = D_o \times \left[\frac{V}{V + \mathrm{SSD} - 100 + t}\right]^2 \times \overline{\mathrm{CF}} \times \overline{\mathrm{TPR}}_{d+b} \quad (3).$$

Two other aspects of our methods should be mentioned. The field shape is entered into a treatment-planning computer using a digitizer which enables us to provide the workshop with a real-size diagram to produce the cutout. The input may be in the form of X-ray films at any magnification factor, and not necessarily perpendicular to the central axis of the beam. We have also considered the need for good quality documentation for the patient's chart and the output of the program is plotted on a piece of cardboard, illustrated in Fig. 5. Polaroid™ photographs are attached to this sheet (not shown in this figure). The small diagram is drawn with high precision and has been useful in reconstructing fields at a later date. The multicolour feature of the pen plotter is used to advantage to highlight common groups of information.

Results

An overall test of the program was made on an aperture in clinical use, the shape is shown as an insert to Fig. 6. The depth-dose was measured for the 20 cm open cone in 12 and 20 MeV beams at 104 cm SSD and is shown as a solid line. The depth-dose was then measured with the cutout inserted and is shown as the dashed line. The program was then used to calculate the dose rate at nine points indicated in the figure. The ratio

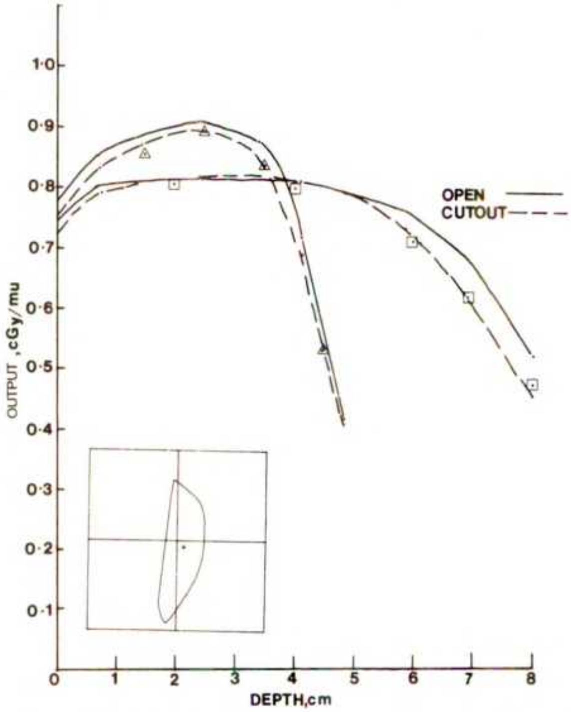


Figure 6. The output against depth, measured for an open cone and with the aperture shown as an insert for 12 and 20 MeV beams. The calculated outputs are shown as points.

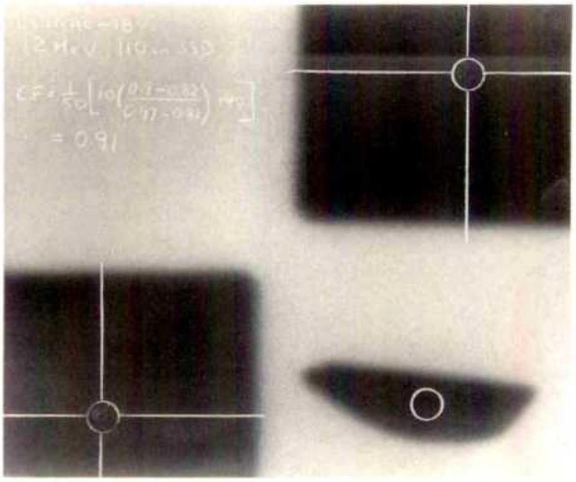


Figure 7. The open cone and cutout exposures on a piece of RP/V film illustrating the technique used to measure the cutout factor.

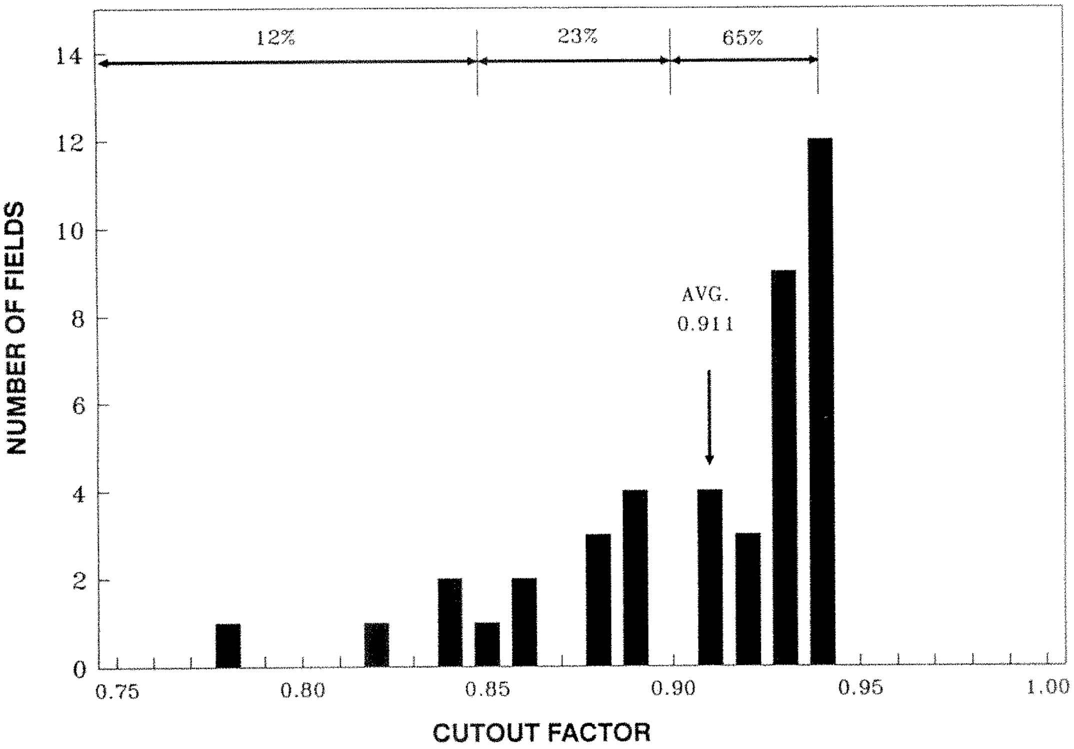


Figure 8. The distribution of calculated cutout factors in 42 electron fields selected from 600 calculations on the basis that the cutout factor was less than 0.95.

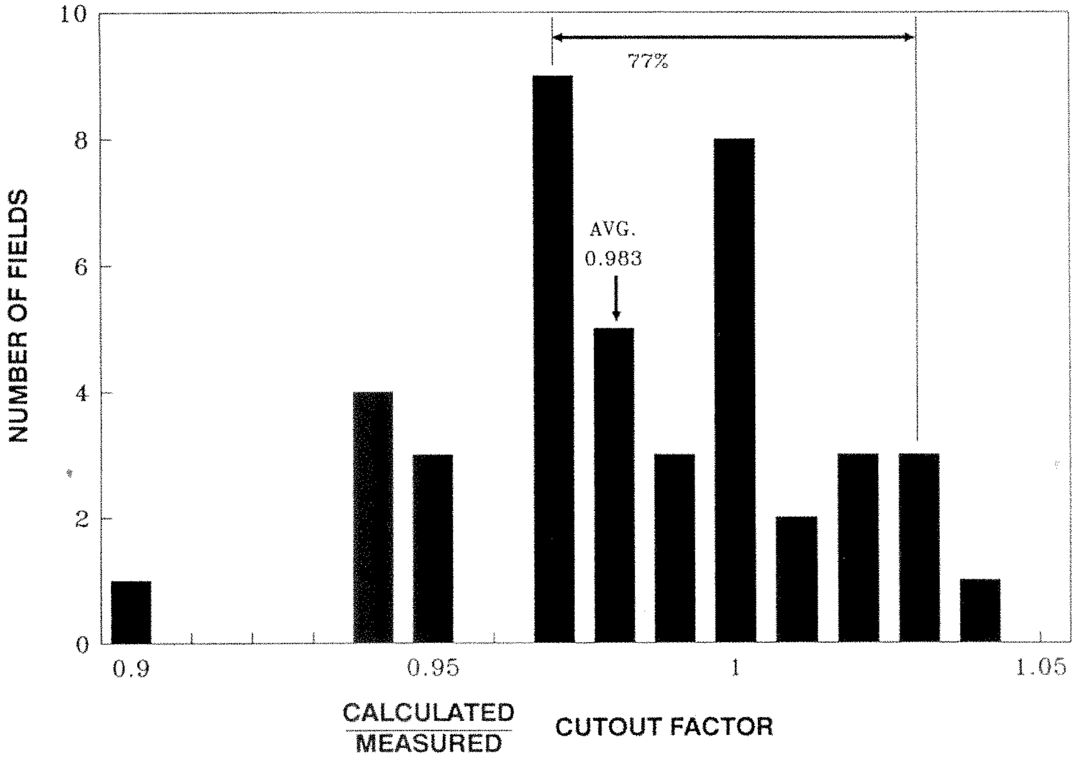


Figure 9. The distribution of the ratio of calculated to measured cutout factors in 42 electron fields.

of the calculated to measured output is 0.994, and the standard deviation is 0.014.

It has been our practice to measure the output factor of an irregular field. The technique is illustrated in Fig. 7 which shows an evaluation of the arrangement shown in Fig. 5. A piece of Kodak RP/V film is placed at 1 cm depth in a tissue-equivalent rubber phantom and exposed to 50 and 40 mu in two locations. The cutout is then installed and an exposure of 50 mu given. The optical density in the open-cone exposures are used to calibrate the film to determine the output in the irregular field.

During the first 14 months of use of the CUTOUT program, approximately 600 calculations were made, and of these, 42 resulted in a cutout factor of less than 0.95, verified by measurement. The calculated cutout factor were as low as 0.77 and distributed as shown in Fig. 8. The ratio of the calculated to measured value is shown in Fig. 9, in which it is shown that the program was accurate to ±3% in 77% of cases.

Discussion

The process of measurement of the output of each irregular electron field is very time consuming and unlike dosimetry procedures employed for photon beams. The computer program described here largely overcomes this problem by providing a calculation method. We have considered it prudent to measure unusual cutouts which we have defined as those with a cutout factor lower than 0.95, but in our experience this amounts to only 7% of the electron fields we employ.

Acknowledgments

We are grateful to Mary Rouzer for her careful preparation of this manuscript and to Andrew Jones for the production of Figs 2, 4, 8 and 9.

References

AAPM Task Group 21 of the Radiation Therapy Committee, 1983. A protocol for the determination of absorbed dose from high-energy photon and electron beams. *Medical Physics, 10,* 741–771.

Biggs, P. J., Boyer, A. L. & Doppke, K. P., 1979. Electron dosimetry of irregular fields on the Clinac-18. *International Journal of Radiation Oncology, Biology, Physics, 5,* 433.

Bruinvis, I. A. D., van Amstel, A., Elevelt, A. J. & van der Laarse, R., 1983. Calculation of electron beam dose distributions for arbitrarily shaped fields. *Physics in Medicine and Biology, 28,* 667–683.

Dutreix, A. & Briot, E., 1985. The development of a pencil-beam algorithm for clinical use at the Institut Gustave Roussy. In *The computation of dose distributions in electron beams. Radiotherapy*, ed. by A. E., Nahum (University of Umeå, Sweden), pp. 242–270.

Khan, R. M., Deibel, F. C. & Berbi, B. J., 1987. Dosimetry of irregularly shaped electron fields. *Medical Physics, 14,* 473.

Kooy, H. M. & Rashid, H., 1989. A three-dimensional electron pencil-beam algorithm. *Physics in Medicine and Biology, 34,* 229–243.

McParland, B. J., 1989. A method of calculating the output factors of arbitrarily shaped electron fields. *Medical Physics, 16,* 88–93.

Mills, M. D., Hogstrom, K. R. & Fields, R. S., 1985. Determination of electron beam output factors for a 20 MeV linear accelerator. *Medical Physics, 12,* 473–476.

Sharma, S. C., Wilson, D. L. & Jose, B., 1984. Dosimetry of small fields for the Therac 20 electron beams. *Medical Physics, 11,* 697–702.

1990, *The British Journal of Radiology*, 63, 65–68

Technical note

Low-field cine magnetic resonance imaging

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The spin warp technique (Edelstein et al, 1980) is now the most commonly used method of image formation for nuclear magnetic resonance (NMR) studies. This technique combines frequency and phase encoding of positional information onto the signal to allow subsequent image reconstruction. Each line of data in a scan is subject to the same frequency-encoding procedure but has a unique amount of phase encoding. Since the sampling is relatively fast, the signal can be considered to be a sample at a particular point in time. For cardiac imaging, we need to ensure that for each phase encoding we are sampling the same point in the cardiac cycle if the final image is to be an accurate representation of that point in the cardiac cycle. This is achieved by synchronizing the data sampling with the patient's electrocardiogram (ECG) signal. If we sample at a number of points in each cardiac cycle, we can acquire a number of images which represent different stages of the cardiac cycle (Fig. 1). These images can then be viewed individually or in the form of a closed loop to enhance the perception of the motion in the images. This technique is commonly referred to as cine NMR or cine magnetic resonance imaging (MRI).

To provide sufficient sampling points within the cardiac cycle, the pulse sequence must have a short repetition time; hence a gradient–echo, rather than a spin–echo, is used. This also has the advantage of enhancing the signal from flowing blood.

Instrumentation

The images were acquired on our 0.08 T (3.4 MHz) resistive system (Redpath et al, 1987) using a 45 × 45 cm field of view. Single slice acquisition without signal averaging was used with a slice thickness of 20 mm and an image matrix of 128 × 128 pixels giving an in-plane resolution of 3.5 mm. The data sampling was 10 kHz in phase and quadrature, giving a sampling period of 12.8 ms. The radio-frequency (RF) excitation pulse was a 90° pulse having a Gaussian slice profile with a full width half-maximum of 1.2 ms. Synchronization to the cardiac cycle was achieved using a conventional 3-lead ECG; the amplifier for the ECG signal was opto-coupled to a standard ECG monitor (Rigel 302) to ensure electrical isolation. On detection of a QRS complex, the monitor initiates a pulse sequence with a minimum delay between the peak of the QRS and the first RF pulse being approximately 10 ms. The inter-pulse interval was chosen so that a 16-image set covered one cardiac cycle without over-running. The minimum interval between the RF pulses was 35 ms, and this could be incremented in 1 ms steps as required.

Methods

Fast ungated gradient–echo saturation–recovery scans were used to position the patient so that the first image set was acquired at the level of the aortic arch. Contiguous sections were then taken through the heart and related vasculature down to the level of the inferior surface of the heart. Typically, seven sections will suffice for this, giving an examination time of around 20–25 min.

Results

Figure 2a shows a set of 16 cine MRI images of one of the authors at the level of the root of the aorta;

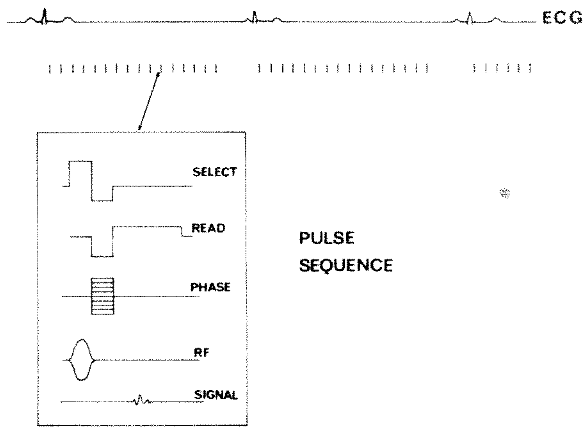

Figure 1. The position of the pulse sequences in relation to the subject's ECG and the gradient waveforms used in the pulse sequence.

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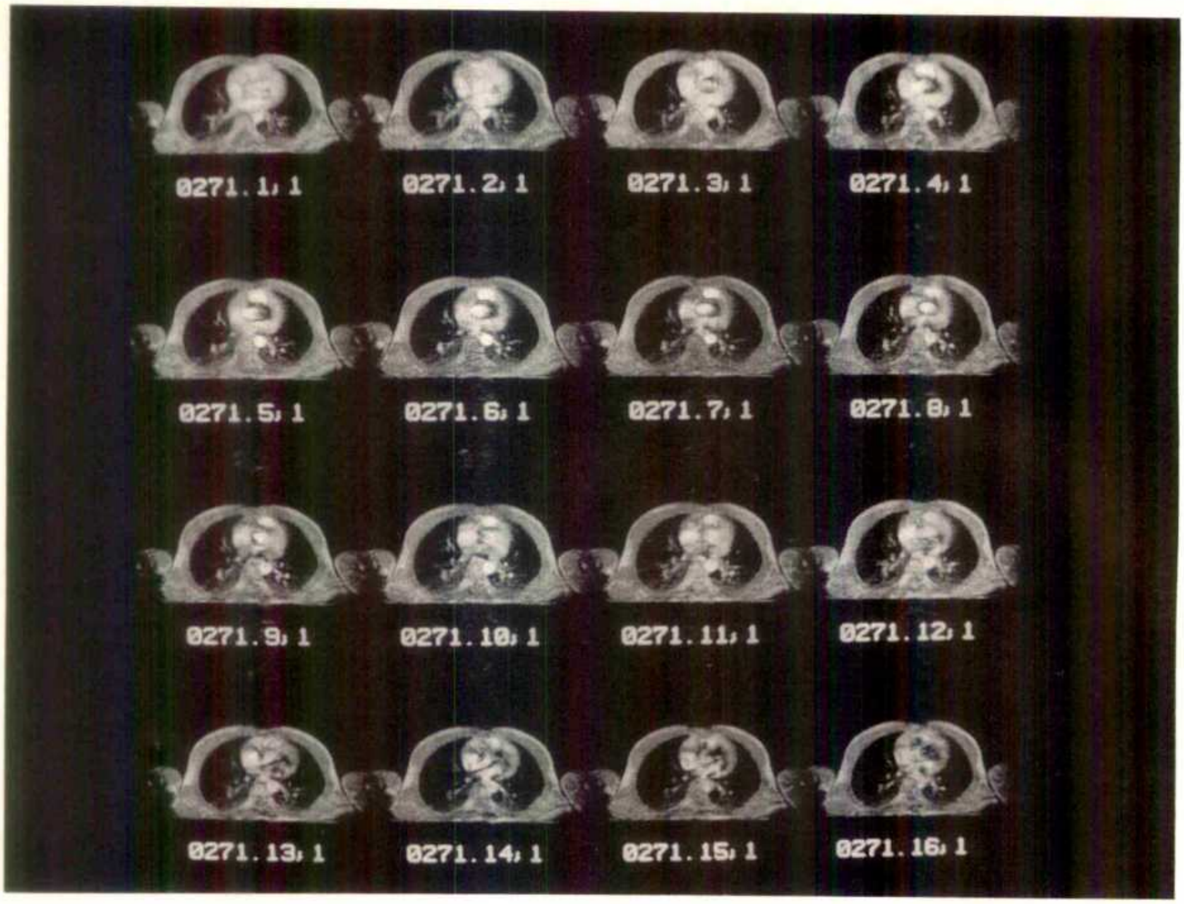
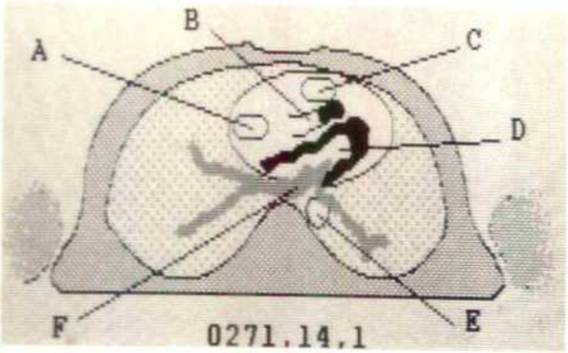
‡Author for correspondence.



(a)



(b)

Figure 2. (a) A set of 16 images, at the level of the aortic arch, covering the whole cardiac cycle of a normal volunteer obtained using an interpulse interval of 60 ms. (b) A line diagram of the major features of frame 14 of the 16-frame image set shown in Fig. 2a. A = venae cavae; B = left ventricular outflow tract; C = right ventricular outflow tract; D = plug flow through mitral valve; E = descending aorta; F = pulmonary vessels.

Fig. 2b is a line diagram of the fourteenth frame of the 16-image set with the major features labelled. The enhanced signal, associated with gradient–echo images of flowing fluid, means that the arterial flow in the ascending aorta, descending aorta, right ventricular outflow tract and various small pulmonary vessels can be clearly seen in frames 4–10. The loss of signal around the periphery of the ascending aorta and just distal to the aortic valve is a result of turbulence associated with the aortic valve, and was seen in all normals. Slight flow enhancement can also be seen in the left atrium in frames 5–15 because of filling from the venae cavae. Filling of the left ventricle from the left atrium is clearly seen in frames 13–15 in the form of a tongue extending into the left ventricle. Frames 1 and 2 offer reasonable definition of the cardiac chambers. The duration of

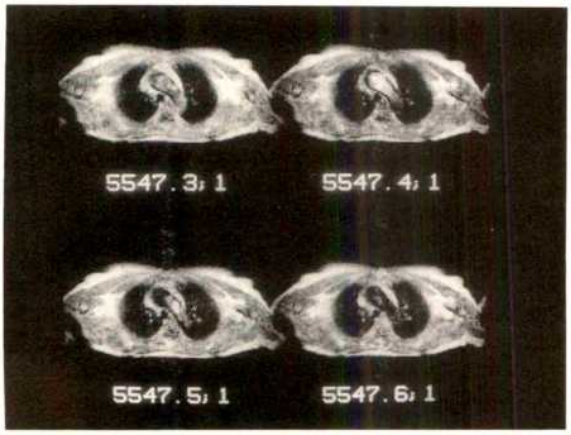


Figure 3. Four frames from a 16-frame cine MRI sequence at a position midway between the aortic valve and arch in a patient suffering from severe aortic stenosis.

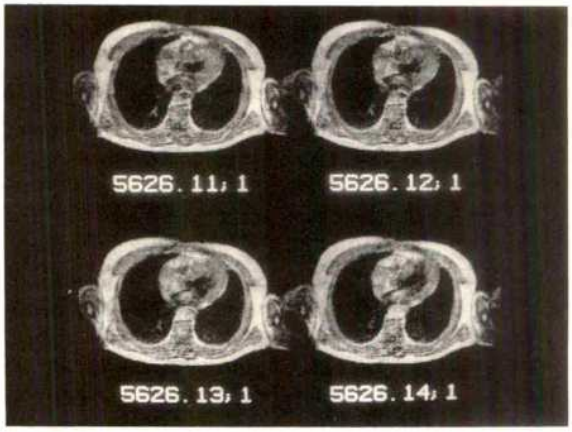


Figure 4. Four frames from a 16-frame cine MRI sequence at the level of the aortic and mitral valves in a patient suffering from moderate aortic regurgitation.

systole can be estimated from the duration of the flow enhancement in the arterial blood. Left ventricular wall motion can also be assessed by viewing the frames in a cine loop.

In normal subjects, aortic flow becomes non-turbulent approximately 20 mm above the aortic valve resulting in signal enhancement, turbulence in the aorta being indicative of aortic stenosis. Figure 3 shows four successive frames from a 16-frame cine MRI set with the first of the four frames representing the start of systole. The following three frames show a progressive loss of signal in the aortic arch as a result of severe turbulence induced by aortic stenosis. Aortic or mitral regurgitation can also be detected from the presence of turbulent backflow from the valve. Figure 4 shows four frames from a 16-frame cine MRI sequence starting at frame 11 with the subsequent frames being at 40 ms intervals. Aortic regurgitation causes the signal void, which can be seen extending into the left ventricle prior to normal filling from the left atrium (frames 13 and 14). Figure 5 shows a case of mitral regurgitation where turbulence is seen extending into the left atrium through the mitral valve during systole. The clinical diagnosis from the cine MRI studies was subsequently confirmed from cardiac catheterization data.

The diagnosis of aortic stenosis and valve disease was generally improved by viewing the frames as a cine loop rather than as individual frames, since the perception of motion allowed more accurate assessment of cardiac function.

Discussion

Fast partial-saturation scans using gradient reversal to form the echo are subject to strong signal enhancement from non-turbulent flow of material into the image slice. The enhancement arises from the fact that this material has not experienced any previous RF pulses and hence contributes a full unsaturated signal, with maximum enhancement occurring when the flow is perpendicular to the image plane. To make best use of this artefact in cine MRI requires the flow in the vessel or chamber of interest to have a component which is perpendicular to the imaging plane, hence the use of transaxial planes. While it is possible to use oblique planes to give true short and long axis views, the setting-up procedure tends to be lengthy (Bernstein et al, 1986). When flow occurs in the presence of field gradients, a phase shift is induced (Van Dijk, 1984), the size of which depends on the velocity. In the case of turbulent flow, a wide range of velocities are present, leading to phase shifts over the full range of 0–2, so that little or no net signal results. Reducing the resolution (pixel size) increases the phase shift for a given velocity; however, since the phase spread will be accumulated across a smaller area, the sensitivity to turbulence is often reduced.

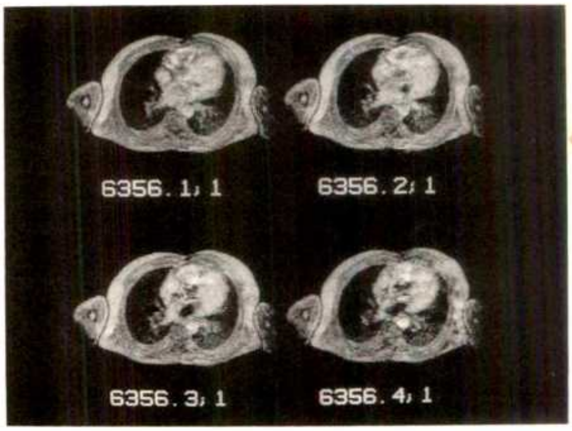


Figure 5. Four frames from a 16-frame cine MRI sequence at the level of the mitral valve in a patient with moderate mitral regurgitation.

Since our implementation of cine MRI produces a "burst" of 16 pulses following a QRS complex and then a variable delay (depending on the heart rate) to the next QRS, the signal intensity will vary through the 16-image set owing to the variable recovery time between the end of one "burst" and start of the next "burst". The form of this variation depends on the flip angle used, since larger flip angles have a swifter approach to an equilibrium state. Some distortion of the slice profile is inherent in all fast two-dimensional imaging, but the use of a smaller flip angle reduces this distortion (Frahm et al, 1987). However, a smaller flip angle will tend to reduce the contrast between the flowing blood and static tissue. Our implementation of cine MRI also precludes the use of steady-state-free precession (SSFP) techniques to improve the signal-to-noise ratio (SNR), since a genuine steady state is not established. Only if a "free-running" sequence is used in conjunctioin with retrospective gating (Plugfelder et al, 1988), can SSFP sequences be used.

Scaling the images (so that the full output range is used) is usually done by scaling to the maximum signal. This is not advisable for cine MRI, since the maximum signal is generally a result of flow enhancement and so the scaling will vary during the cardiac cycle, leading to varying intensities for static tissues. Using a constant scale factor also produces changes in intensity during the cycle because of the variable recovery period between the "bursts" of pulses. The use of a constant scale factor produces an image set in which the first few scans have significantly higher signal levels producing a "lightning-flash" effect when viewed in a cine loop. Our images were scaled such that the thoracic adipose tissue is at a set level and scale the rest of the image relative to this. While this may lead to some truncation of the flow-enhanced signals, it does not seem to affect the diagnostic utility of the images.

The resolution of the transaxial scans could be improved by sampling more points from each gradient–echo and by reducing the field of view (FOV) in the phase-encoding direction. Thus instead of acquiring a 128 × 128 square matrix with a 45 cm FOV, a 128 × 256 matrix with a 30 × 60 cm FOV could be acquired, with phase encoding in the anterior–posterior direction. In this case, the data sampling interval is increased from 12.8 ms to 25.6 ms on our system. Only the central 128 points of each line are retained after processing to give a 128 × 128 matrix with a 30 × 30 cm FOV for the final image.

The reduction in signal resulting from the reduced pixel size and increased echo time is only partially compensated for by the increased number of samples, unless only a very modest improvement in resolution is used. In addition, whilst the scan time is unchanged, the repetition time of each line is increased so the temporal resolution will be reduced and artefacts resulting from motion during the sampling period will be increased.

In conclusion, despite the relatively poor resolution of these scans, they allow both cardiac anatomy and function to be visualized and give a high sensitivity to turbulence.

References

BERNSTEIN, M. A., PERMAN, W. H., BESOZZI, M. C. & THOMASSON, D. M., 1986. Pulse-sequence-generated oblique magnetic resonance imaging: application to cardiac imaging. *Medical Physics, 13(5)*, 648–657.

EDELSTEIN, W., HUTCHISON, J. M. S., JOHNSON, G. & REDPATH, T. W., 1980. Spin warp NMR imaging and application to human whole body imaging. *Physics in Medicine and Biology, 25*, 751–756.

FRAHM, J., HANICKE, W. & MERBOLDT, K. D., 1982. Transverse coherence in rapid FLASH NMR imaging. *Journal of Magnetic Resonance, 72*, 307–314.

PLUGFELDER, P. W., SECHTEM, U. P., WHITE, R. D. & HIGGINS, C. B., 1988. Quantification of regional myocardial function by rapid cine-MRI imaging. *American Journal of Roentgenology, 150*, 523–529.

REDPATH, T. W., HUTCHISON, J. M. S., EASTWOOD, L. M., SELBIE, R. D., JOHNSON, G., JONES, R. A. & MALLARD, J. R., 1987. A low field NMR imager for clinical use. *Journal of Physics E: Scientific Instruments, 20*, 1228–1234.

VAN DIJK, P., 1984. Direct cardiac NMR imaging of heart wall and blood flow velocity. *Journal of Computer Assisted Tomography, 8*, 429–436.

1990, *The British Journal of Radiology*, 63, 69–72

Case reports

Aneurysms involving the intrapetrous internal carotid artery: a rare cause of Horner's syndrome

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Aneurysms involving the intrapetrous carotid artery are a rare cause of Horner's syndrome and only three cases appear to have been described previously. These aneurysms vary in their mode of clinical and radiological presentation depending on the direction of expansion of their sac. Non-invasive radiological investigation may demonstrate striking abnormalities, but the definitive diagnosis can only be made by angiography.

Case reports

Case 1

A 19-year-old woman who was 34 weeks pregnant complained of an attack of severe migrainous headache, which had left her with a drooping left eyelid. This attack was similar to many she had experienced since the age of 8 years, but none previously had been followed by neurological deficit. She gave no history of head injury or middle ear infection. Examination revealed left Horner's syndrome, in addition to partial left 8th, 9th and 10th cranial nerve palsies. All other tests were normal. Radiological investigation was deferred until she had delivered her baby.

Plain radiographs of the skull base (Fig. 1) showed a large area of pressure erosion of the medial half of the floor of the left middle cranial fossa with a scalloped margin. Unenhanced axial computed tomographic (CT) sections defined a soft-tissue mass impressing the nasopharynx and obliterating the left fossa of Rosenmuller. Magnetic resonance imaging (MRI) confirmed the presence of a mass lesion eroding the base of the skull in the region of the carotid canal (Fig. 2). The signal characteristics indicated that it was composed of either calcium or flowing blood; considering the plain radiographs and CT, the appearances suggested a diagnosis of an intrapetrous aneurysm. Left carotid angiography revealed a giant fusiform aneurysm of the intrapetrous segment of the internal carotid artery (Fig. 3). The patient withstood operative exploration and ligation of the internal carotid artery without complication.

Case 2

A 61-year-old housewife gave a history of attacks of headaches and right nasal hemianopia for 10 years, which had been diagnosed as migraine. Recently, she had experienced bouts of pain of varying severity behind the right eye. Physical examination revealed a mild right proptosis and a right Horner's syndrome. No bruit was heard. No other cranial nerves were

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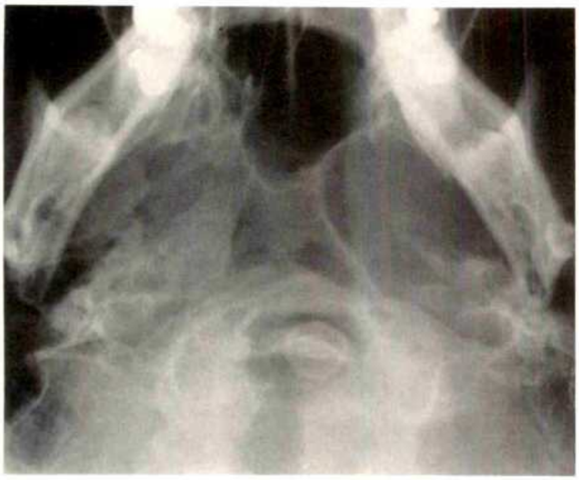


Figure 1. *Case 1.* Conventional radiograph of the skull base, showing extensive erosion of the floor of the middle cranial fossa and petrous apex.

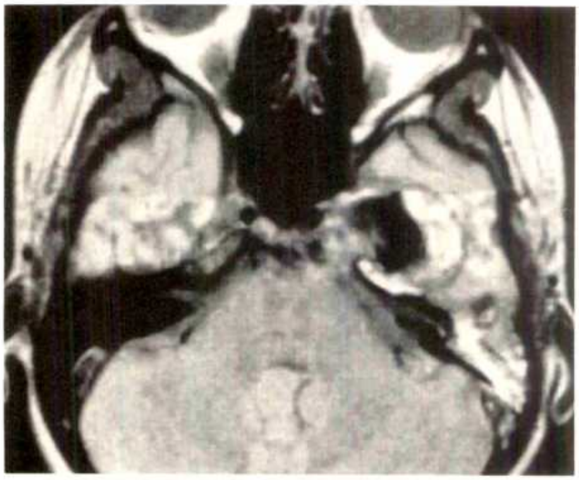


Figure 2. *Case 1.* Magnetic resonance axial image (SE 500/27) confirming the presence of a basal skull mass lesion, the centre of which has a signal void consistent with flowing blood.

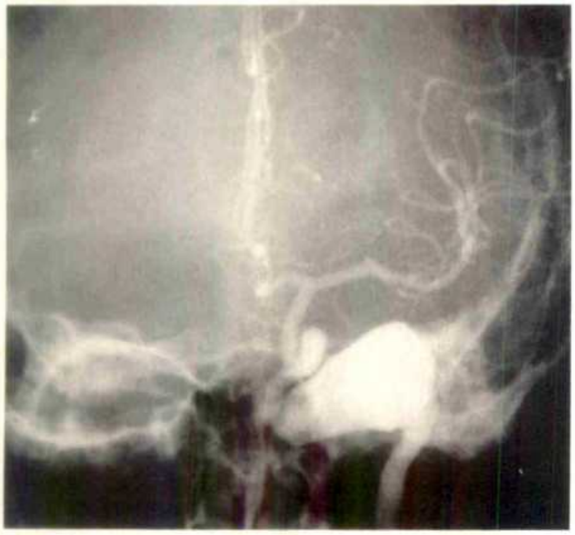


Figure 3. *Case 1.* Antero-posterior view after selective injection of the left internal carotid artery, outlining a large fusiform aneurysm of the intrapetrous segment.

involved. The patient was normotensive and blood tests were normal.

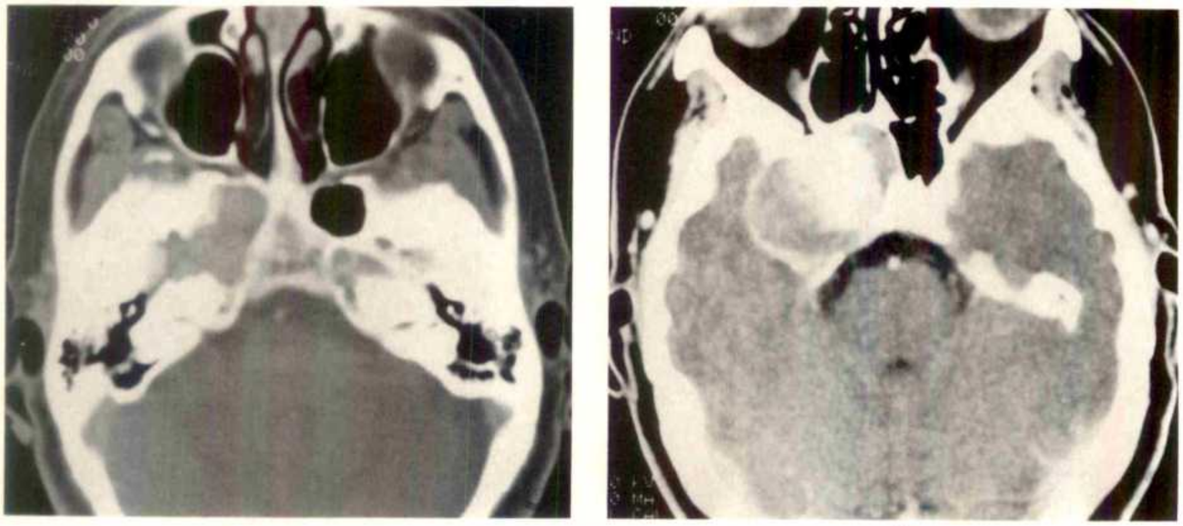
Skull radiographs showed erosion of the right petrous apex and the adjacent part of the body of the sphenoid bone. Axial CT scans confirmed this finding and demonstrated a vividly but irregularly enhancing mass arising out of the right carotid canal and extending into the parasellar region (Fig. 4). The diagnosis was made of a partially thrombosed aneurysm of the intracavernous internal carotid artery with proximal extension to involve the intrapetrous segment. An angiogram was not performed as the patient's symptoms had improved; she is being managed expectantly.

Discussion

Aneurysms of the internal carotid artery most frequently take the form of fusiform widening of the proximal few centimetres in the neck or of "berry" lesions of the cavernous part or siphon; they seldom occur on that portion of the artery that lies within the petrous temporal bone. A review of the literature yielded only 32 reported cases, with patients ranging in age from 7 to 65 years and men and women being equally affected. The most frequent neurological deficit present in 19 of the 32 cases was dysfunction of the auditory nerve. Other cranial nerves were sometimes affected, but there are only three cases recorded in which the sympathetic fibres to the orbit were involved (Hardin & Snodgrass, 1964; Wemple & Smith, 1966, Blom, 1985).

The sympathetic fibres supplying the orbit emerge from the spinal cord at the cervico-dorsal junction, relay in the superior cervical ganglion and ascend with the carotid arteries to supply the contents of the orbit. Interruption of these fibres will result in the syndrome described by Horner in 1869, of a constricted pupil, ptosis and if the lesion is proximal to the carotid bifurcation, facial anhydrosis.

Of the many causes of Horner's syndrome described, aneurysms of the skull base are among the least common. The syndrome is a recognized complication of migraine, being caused by damage to the sympathetic fibres within the carotid artery sheath when the vessel dilates during an attack (Walton, 1985). Although both patients described in this paper had migrainous head-



(a)

(b)

Figure 4. *Case 2.* (a) Unenhanced axial CT scan showing a soft-tissue mass eroding the floor of the middle cranial fossa and petrous apex. (b) Post-injection slice at a higher level shows vivid inhomogenous enhancement within the mass, the largest component of which lies in the parasellar region with erosion of the sphenoid.

Table I. Clinical manifestations

Direction of expansion	Structure affected	Clinical presentation
Medial	Cavernous sinus, including 3rd, 4th and 6th cranial nerves; nasopharynx	Diplopia, nasopharyngeal mass
Lateral	Middle ear, eustachian tube, cochlea and semicircular canals; 7th and 8th cranial nerves	Hyperacusis, deafness, dizziness. Mass behind eardrum. Ear/nasal haemorrhage
Superior/anterior	Trigeminal ganglion; foramina ovale and spinosum	Trigeminal neuralgia
Inferior	Jugular foramen and hypoglossal canal; 9th, 10th and 12th cranial nerves	Lower cranial nerve palsies
Posterior	Dura of posterior cranial fossa, 7th and 8th cranial nerves	Headaches, facial palsy and deafness

Note: A Horner's syndrome may be present with any of the examples given.

aches, it seems likely that they were produced in each by the aneurysm itself rather than by dilatation of the carotid within its sheath. Indeed, the mechanism of the sympathetic paralysis may be similar, since an aneurysmal sac corresponds to a state of persistent dilatation of a segment of the artery.

The aetiology of intrapetrous aneurysms is obscure and usually there is no obvious cause; most cases are labelled as congenital anomalies (Brihaye, 1979). Atherosclerosis, responsible for the majority of extracranial carotid aneurysms (Rittenhouse et al, 1972), appears to spare the petrous portion (Samuel, 1956). Furthermore, 22 (70%) of the 32 reported cases were in patients aged under 40 years. Other potential causes are head trauma, middle ear sepsis and surgery. Three patients had sustained severe closed head injuries 6–24 months prior to presentation (Pecker et al, 1960; Busby et al, 1968; Teal et al, 1973). Only one showed a fracture line, but basal skull fractures are notoriously difficult to identify radiologically. Three patients gave histories of middle ear sepsis (Hiranandani et al, 1962; Allegre et al, 1966; Stallings & McCabe, 1969). One case occurred after mastoidectomy (Barrett & Lawrence, 1960).

The clinical presentation will vary according to the direction of expansion of the aneurysmal sac (Table I), and it may be anticipated from a study of the anatomy of the carotid canal (Fig. 5). An erroneous diagnosis of glomus jugulare tumour, particularly in female patients, may be prompted by signs referable to the middle ear, sometimes with evidence of blood or a vascular mass behind the tympanic membrane (Brihaye, 1979). Although the sympathetic fibres form a plexus around the internal carotid artery, Horner's syndrome appears to be very rare. Glossopharyngeal and vagal palsies have only once been previously reported (Guirguis & Tadros, 1961), a surprising finding considering the close proximity of these nerves to the intrapetrous carotid. Their point of exit from the skull, the jugular foramen, is situated just beneath and posterior to the carotid canal (Fig. 5).

Carotid angiography remains the definitive method of diagnosis but other techniques may identify the lesion and provide clues to its nature. Conventional radiographs in 17 out of 28 patients (including the two cases reported here) demonstrated erosion of the petrous temporal bone. The site of erosion is related to the direction of expansion of the aneurysm and corresponds to the clinical signs. A basal skull fracture, if identified, may have aetiological significance (Morantz et al, 1976). Enhanced CT may be useful, as in Case 2. Magnetic resonance imaging, of proven value in the diagnosis of giant intracranial aneurysms (Olsen et al, 1987), made a useful contribution to the diagnosis in Case 1, revealing a mass eroding the skull base with a central signal void

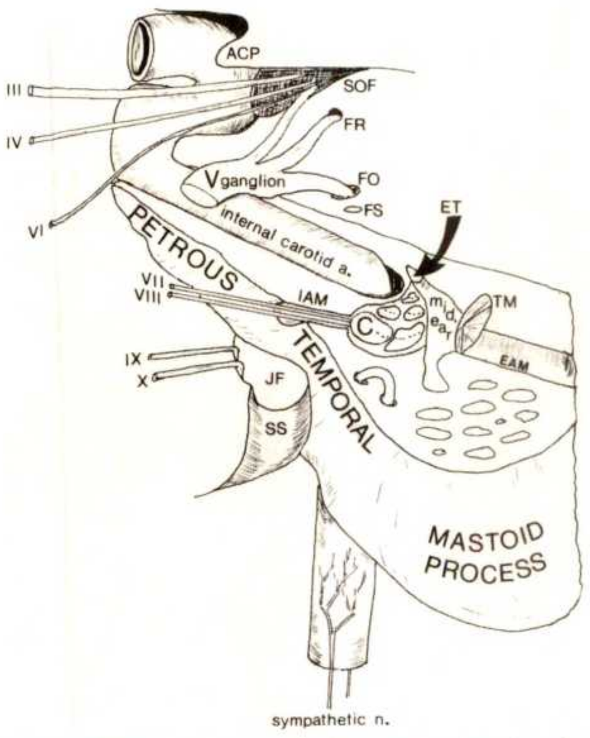


Figure 5. Schematic diagram of a horizontal section through the right petrous temporal bone to demonstrate the anatomy of the carotid canal. ACP, anterior clinoid process; C, cochlea; EAM, external auditory meatus; ET, eustachian tube; FO, foramen ovale; FR, foramen rotundum; FS, foramen spinosum; IAM, internal auditory meatus; JF, jugular foramen; SOF, superior orbital fissure; SS, sigmoid sinus; TM, tympanic membrane.

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compatible with flowing blood and consistent with an aneurysm. Retained secretions secondary to obstruction of the eustachian tube (the mass had obliterated the adjacent fossa of Rosenmuller) is the likely explanation for the high signal from the mastoid and mesotympanum.

Acknowledgments

We would like to thank the Department of Teaching Media for preparing the illustrations from the original radiographs. We are also grateful for the help and advice given by Dr E. Burrows in the preparation of the manuscript.

References

Allegre, G., Aimard, G. & Dechaume, J. P., 1966. Une nouvelle observation d'aneurisme intrapétreux de la carotide interne à sémiologie ectopique. *Revue Neurologigue*, *115*, 1052–1055.

Barrett, J. H. & Lawrence, V. L., 1960. Aneurysm of the internal carotid artery as a complication of mastoidectomy. *Archives of Otolaryngology*, *72*, 366–368.

Brihaye, J., 1979. Internal carotid aneurysms arising in the carotid canal. In *Cerebral Aneurysms. Advances in Diagnosis and Therapy*, ed. by H. W. Pia, C. Langmaid & J. Zierski (Springer-Verlag, New York), pp. 55–62.

Blom, R. J., 1985. Intrapetrous intracavernous fusiform aneurysm of the internal carotid artery. *Journal of the Canadian Association of Radiologists*, *36*, 337–340.

Busby, D. R., Slemmons, D. H. & Miller, T. F., 1968. Fatal epistaxis via carotid aneurysm and eustachian tube. *Archives of Otolaryngology*, *87*, 293–296.

Guirguis, S. & Tadros, F. W., 1961. An internal carotid aneurysm in the petrous temporal bone. *Journal of Neurology, Neurosurgery and Psychiatry*, *24*, 84–85.

Hardin, C. A. & Snodgrass, R. G. 1964. Dissecting aneurysm of the internal carotid artery treated by fenestration and graft. *Surgery*, *55*, 207–209.

Hiranandani, L. H., Chandra, O., Malpani, N. K. & Ahuja, K. K., 1962. An internal carotid artery aneurysm in the petrous temporal bone. *Journal of Laryngology and Otology*, *76*, 703–706.

Horner, F., 1869. Ueber eine form von ptosis. *Klin. Monatsbl. Augenheilta*, *7*, 193–198.

Morantz, R. A., Kirchner, F. R. & Kishore, P., 1976. Aneurysms of the petrous portion of the internal carotid artery. *Surgical Neurology*, *6*, 313–318.

Olsen, W. L., Brant-Zawadzki, M., Hodes, J., Norman, D. & Newton, T. H., 1987. Giant intracranial aneurysms: MR imaging. *Radiology*, *163*, 431–435.

Pecker, J., Hoel, J. & Javelet, A., 1960. Paralysie du moteur oculaire externe par aneurysme intra-pétreux traumatique de la carotide interne. *La Presse Médicale*, *68*, 1023–1026.

Rittenhouse, E. A., Radke, H. M. & Sumner, D. S., 1972. Carotid artery aneurysm: review of the literature and report of a case with rupture into the oropharynx. *Archives of Surgery*, *105*, 786–789.

Samuel, K. C., 1956. Atherosclerosis and occlusion of the internal carotid artery. *Journal of Pathology and Bacteriology*, *71*, 391–401.

Stallings, J. O. & McCabe, B. F., 1969. Congenital middle ear aneurysm of the internal carotid. *Archives of Otolaryngology*, *90*, 65–69.

Teal, J. S., Bergeron, R. T., Rumbaugh, C. L. & Segall, H. D., 1973. Aneurysms of the petrous or cavernous portions of the internal carotid artery associated with nonpenetrating head trauma. *Journal of Neurosurgery*, *38*, 568–574.

Walton, J., 1985. Migraine. In *Brain's Diseases of the Nervous System*, 9th edn (Oxford University Press, Oxford), p. 182.

Wemple, J. B. & Smith, G. W., 1966. Extracranial carotid aneurysm: report of four cases. *Journal of Neurosurgery*, *24*, 667–671.

The radiology of Coffin–Lowry syndrome

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The Coffin–Lowry syndrome is a rare disorder inherited as an X-linked condition, affecting men much more severely than women. The characteristics are mental retardation, skeletal abnormalities with short stature, hypermobile joints, loose skin, tapering fingers and dysmorphic facial features.

Case report

The proband was referred for genetic assessment at the age of 15 years because of developmental delay with dysmorphic features. He was the first child of unrelated parents, and had a younger sister. His mother was said to be mildly educationally subnormal, but she came from a family of highly educated people, and there was no other family history of retardation (Fig. 1). His sister (aged 16 years) was of normal intelligence and had no dysmorphic features.

The proband was induced at 36 weeks gestation because of placenta praevia in an otherwise normal pregnancy, and was healthy at birth (birth weight 5 lb 2 oz). His milestones were delayed, sitting at 18 months and only walking at 3 years of age, and making no meaningful sounds until the age of 2 years. He went into residential care for the moderately to severely retarded from 5 years of age, at which time he only had two or three words of speech.

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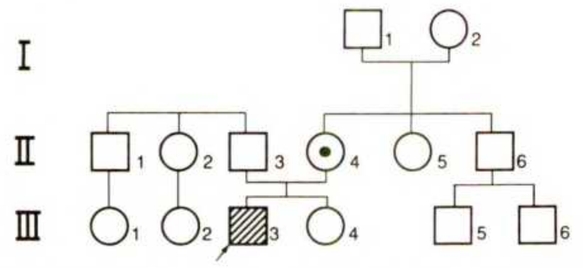


Figure 1. Pedigree of proband. III3 indicates proband; II4 indicates his mother.

In his early teens he developed epilepsy in the form of "drop attacks", which caused him to fall backwards to the ground; he would rise immediately afterwards.

On examination at 15 years of age, he was a thin boy, 154 cm tall (3rd percentile for age) and his span was 154 cm. His head circumference was 54 cm (just below the 50th percentile), inner canthal distance 2.5 cm (3rd percentile) and outer canthal distance 8 cm (3rd percentile). The face (Fig. 2a) was long and thin, with heavy eyebrows, a thick lower lip and a slightly receding chin. His ears were simple and prominent and there was relative maxillary hypoplasia. There was a short philtrum. He had a high, wide bridge to his rather large nose, which was deviated to the left. His eyes were normal on ophthalmological examination (including normal fundi), but there was a slight divergent squint. There was an antimongoloid slant to the palpebral fissures but no hypertelorism. The upper incisors had fallen out, said to have been due to abnormal roots. The remaining teeth were irregular and his palatal arch was rather high.

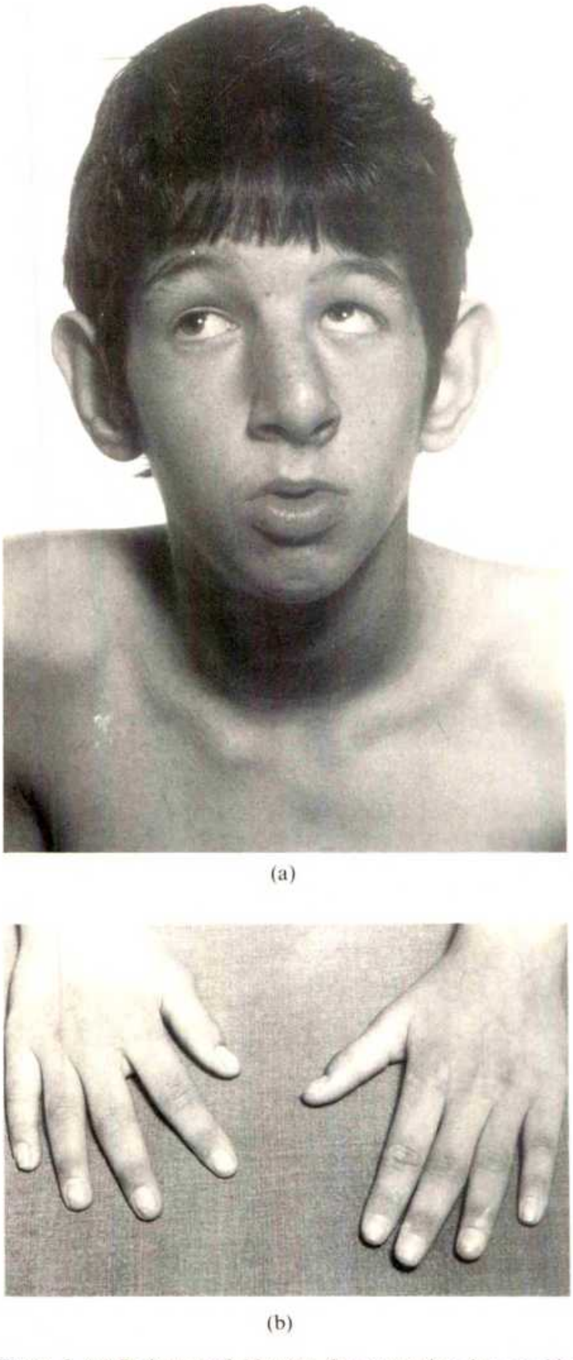
He had marked ligamentous laxity. The hands were large and fleshy, and showed distinct tapering of the fingers (Fig. 2b). Palmar creases were normal. His feet had flat arches, and his second and third toes were of equal length. His chest, abdomen and genitalia were unremarkable.

Investigations showed normal chromosomes 46 XY (with no fragile X chromosomes). Serum and urinary amino acids were normal, as were urinary organic acids and mucopolysaccharides. Thyroid function tests were normal.

Hand and wrist radiographs showed drumstick-shaped terminal phalanges and a short distal ulna (Fig. 3). The metacarpal index was at the upper end of the normal range at 8.2 (normal range 5.4–7.9). The bone age was normal. The spine was markedly abnormal with a lumbar scoliosis. The vertebral bodies were abnormal with a concave anterior aspect and a deficiency in the epiphyseal ring antero-superiorly (Fig. 4). Mid- and upper lumbar vertebrae were most affected. The end plates were irregular. Posterior vertebral arches were normal. The skull (Fig. 5) was abnormal with microcrania, relative frontal bone thickening and maxillary hypoplasia.

The proband's mother was mildly mentally retarded with short stature and an abnormal shuffling gait. There was a history of back pain. She had never had epileptic fits. She was able to cope with simple household tasks but did not have a job. On examination, she was slim, with a height of 154 cm (10th percentile) and span of 153 cm. She had slight curvature of the spine in the lumbar region with limitation of spinal flexion. The face was long and she had prominent ears. She had very carious teeth, and her palate was slightly high-arched. She had very lax joints. Her fingers were tapering, rather fleshy proximally and thin distally, and her nails were brittle.

Her lumbar spine radiographs showed a scoliosis and a relative increase in height to antero-posterior diameter of the vertebral bodies (Fig. 6).


(a)

(b)

Figure 2. (a) Patient aged 15 years demonstrating dysmorphic features. (b) Patient's hands showing fleshy appearances with distinct tapering of the fingers.

The proband's sister had normal radiographic findings of hands and vertebrae.

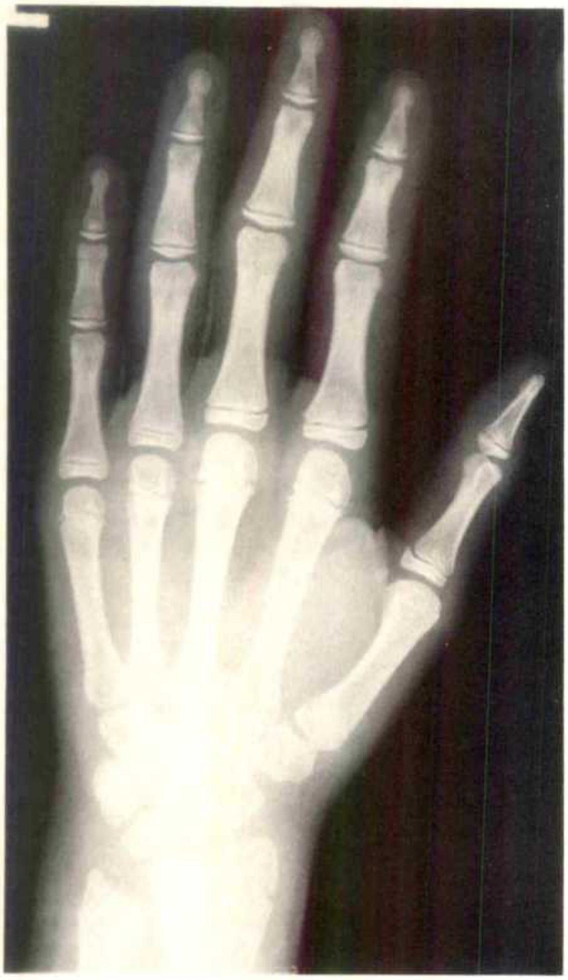


Figure 3. Radiograph of patient's left hand showing drumstick-shaped terminal phalanges.

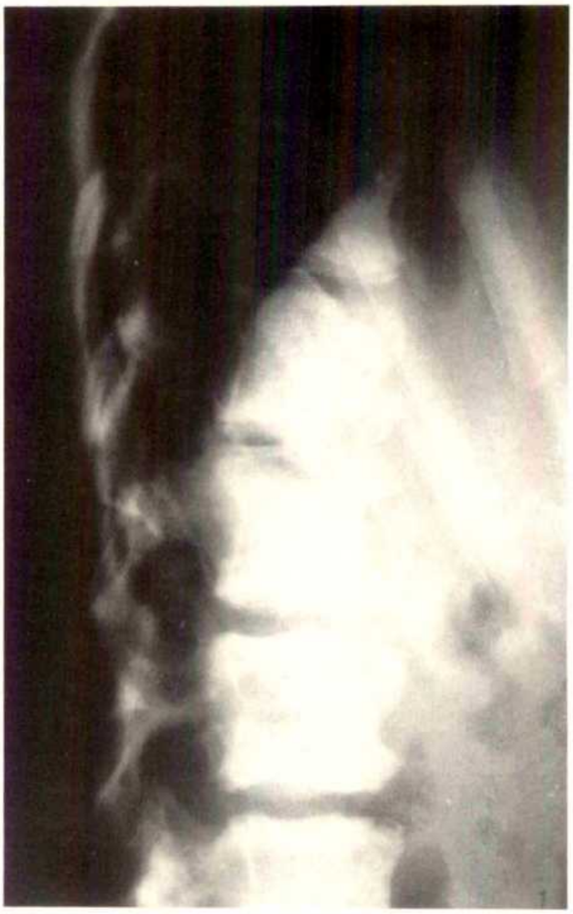


Figure 4. Radiograph of patient's thoraco-lumbar spine. The vertebral bodies are abnormal with an anterior concavity and abnormal end plates.

Discussion

Coffin described a syndrome of mental retardation and associated somatic abnormalities in 1966 (Coffin et al, 1966). Independently, Lowry described the same syndrome in 1971 (Lowry et al, 1971). Temtamy et al (1975) suggested that these were the same entity and coined the name "Coffin–Lowry syndrome". Affected males have severe manifestations and a possible excess of early deaths of male offspring and of abortions has been commented on in the progeny of female carriers (Lowry et al, 1971; Procopis et al, 1972; Temtamy et al, 1975; Gilgenkrantz et al, 1988). Females are variably affected, with some degree of short stature, impaired IQ and some of the characteristic facial and skeletal changes, as seen in this patient's mother. The inheritance is probably of X-linked semidominant type, with females who are mildly affected being at risk of giving birth to severely affected males. No affected male has been known to have had children, so that male-to-male

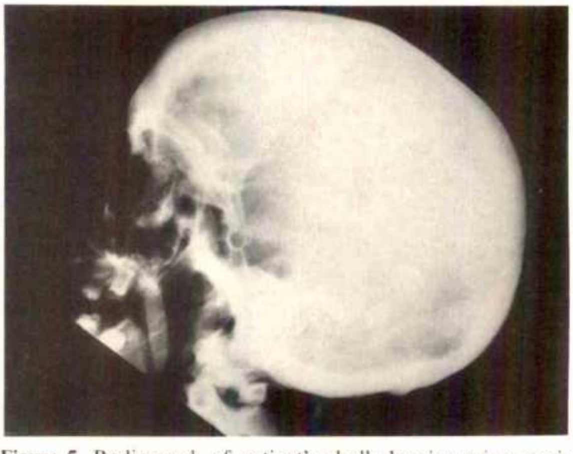


Figure 5. Radiograph of patient's skull showing microcrania and relative frontal bone thickening.

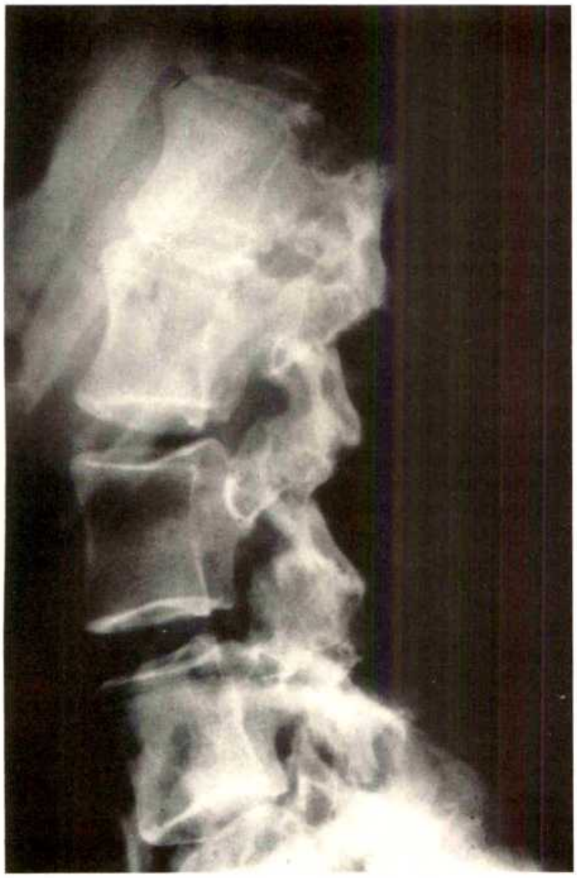


Figure 6. Radiograph of upper lumbar vertebrae of patient's mother showing increased height.

transmission has not been possible, and autosomal dominant inheritance, with females being less severely affected, is still a possibility. Linkage analysis has recently provided evidence in favour of the X-linked mode of inheritance for this condition (Partington et al, 1988).

In the male, the features are those seen in the proband (including heavy eyebrows, prominent nose and thick lower lip), with soft skin, fleshy tapering fingers, ligamentous laxity and severe mental retardation. Hypertelorism and pectus carinatum, not seen in this case, are often present, and the affected individual displays an abnormal posture with an inability to stand fully erect (Gilgenkrantz et al, 1988). Cardiac abnormalities, including mitral valve prolapse, have been described (Temtamy et al, 1975; Hunter et al, 1982). Histological abnormalities were described in the original case report (Coffin et al, 1966) with disordered chrondrocytes in the epiphyses and greatly reduced amounts of elastic fibres in the skin. However, other workers have not confirmed this defect in elastic tissue (Temtamy et al, 1975; Hunter et al, 1982). Since then, extracellular accumulation of abnormal proteodermatan sulphate, produced by skin fibroblasts, has been demonstrated in tissue culture from three patients with Coffin–Lowry syndrome (Beck et al, 1983). This has been postulated as the basic defect at cellular level causing the skin and other connective tissue changes. A connective tissue disorder would be an attractive explanation for the association of skin, bone, joint and cardiac abnormalities.

The radiographic signs are distinctive, and provide helpful confirmation of the diagnosis of this syndrome. The finding of radiographic abnormalities in more mildy affected carrier females is useful for genetic counselling. It would be helpful to know whether carriers of this gene have ever been seen with normal radiographic findings. If not, this would allow confident re-assurance to be given to females at risk of being carriers, who have no abnormalities detectable on radiology, as in the case of the proband's sister.

In the family described here, the proband's mother probably has a new mutation for the Coffin–Lowry syndrome, as there is no other family history of this condition.

References

Beck, M. J., Gloss, J., Ruser, R. & Kruse, H., 1983. Abnormal proteodermatan sulphate in three patients with Coffin–Lowry syndrome. *Paediatric Research*, *17*, 926–929.

Coffin, G. S., Siris, E. & Wegienka, L. C., 1966. Mental retardation with osteocartilaginious anomalies. *American Journal of Diseases of Children*, *112*, 205–213.

Gilgenkrantz, S., Mujica, P., Gruer, P., Tridon, P., Schweitzer, F., Nivelon-Chevallier, A., Nivelon, J. L., Couillault, G., David, A., Lambotte, C., Piussan, C. H. & Mathieu, M., 1988. Coffin–Lowry syndrome: a multicentre study. *Clinical Genetics*, *34*, 230–245.

Hunter, A. G., Partington, M. W. & Evans, J. A., 1982. The Coffin–Lowry syndrome. Experience from four centres. *Clinical Genetics*, *21*, 321–335.

Lowry, B., Miller, J. R. & Fraser, F. C., 1971. A new dominant gene mental retardation syndrome: association with small stature, tapering fingers, characteristic facies and possible hydrocephalus. *American Journal of Diseases of Children*, *121*, 496–500.

Partington, M. W., Mulley, J. C., Sutherland, G. R., Thode, A. & Turner, G., 1988. A family with the Coffin–Lowry syndrome revisited: localisation of CLS to Xp21-pter. *American Journal of Medical Genetics*, *30*, 509–521.

Procopis, P. G., Turner, B. & Ryde, N., 1972. Mental retardation, abnormal fingers and skeletal abnormalities: Coffin's syndrome. *American Journal of Diseases of Children*, *124*, 258–262.

Temtamy, S. A., Miller, J. D. & Hussels-Maunenee, I., 1975. The Coffin–Lowry syndrome: an inherited faciodigital mental retardatic syndrome. *Journal of Paediatrics*, *86*, 724–731.

1990, *The British Journal of Radiology*, *63*, 76

Embolization hazard of laser hot-tip catheters and coated guidewires

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Laser thermal angioplasty is now widely used for the treatment of arterial occlusions or stenoses (Ginsberg et al, 1985; Cumberland et al, 1986; MacCowan et al, 1988). The first commercially available intravascular laser system uses a metal-capped laser fibre to convert the laser energy into thermal energy. New laser catheters for vascular recanalization have been developed, some of which can be used over a guidewire.

Case report

A 56-year-old man presented with left intermittent claudication. An arteriogram revealed a very tight stenosis of the left popliteal artery and diffuse atherosclerotic lesions of the run-off vessels associated with a high-grade stenosis of the origin of the anterior tibial artery and of the tibioperoneal trunk.

Laser-assisted angioplasty was then performed using a 2.5 mm laser catheter (PRL catheter, Trinedyne). This catheter is designed with a central guidewire lumen and a concentric laser tip. The lesions were crossed with a 0.035-inch hydrophilic guidewire (Terumo) because the torque control and slipperiness of the guidewire make it very useful for crossing tight stenoses (Takayasu et al, 1988). The laser catheter was coupled to an Nd-YAG laser source and the first lesion was crossed (12 W for 4 s).

After the energy was applied, removal of the guidewire was difficult; both catheter and guidewire were retrieved. When the guidewire was removed, it was noted that the hydrophilic coating was stripped away from the wire as a result of thermal damage (Fig. 1). In our patient, the wire was replaced by a standard metal guidewire, and the procedure was successfully completed without complication.

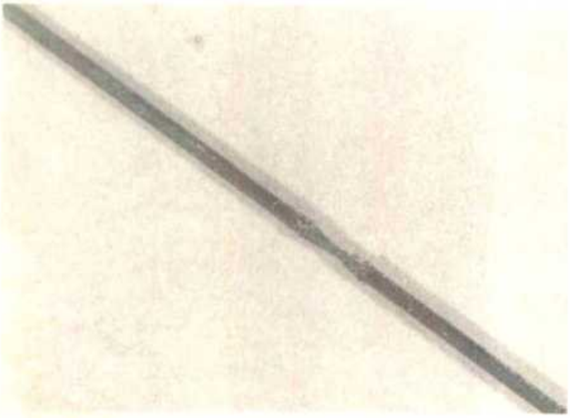

Figure 1. Thermal damage of the hydrophilic coating of a 0.035-inch guidewire because of the laser catheter.

Discussion

Laser angioplasty has proved to be an efficient and safe method for vascular recanalization in some cases. In this method of laser angioplasty we used laser energy which is not applied directly to the tissue but converted into heat in the metal tip. The atheromatous material is ablated by heat radiating from the tip of the catheter, which also causes the guidewire to heat. As a result, we believe plastic-coated guidewires to be incompatible with hot-tip laser angioplasty, and we recommend extreme caution in using any coated guidewire for laser thermal angioplasty. Teflon-coated guidewires have been used in our laboratory at different energy levels without noticeable external damage, but we feel that the use of metallic, non-coated guidewires should be mandatory in order to prevent potential embolization by the guidewire coating.

References

Cumberland, D. C., Sanborn, T. A. & Taylor, D. I., 1986. Percutaneous laser thermal angioplasty: initial clinical results with a laser probe in total periphery artery occlusions. *Lancet*, *i*, 1457–1459.

Ginsburg, R., Wexler, L., Mitchell, R. S. & Profitt, O., 1985. Percutaneous transluminal laser angioplasty for treatment of peripheral vascular disease: clinical experience with 16 patients. *Radiology*, *156*, 619–624.

MacCowan, T. C., Fernis, E. J., Bernes, R. W. & Baker, M. L., 1988. Laser thermal angioplasty for the treatment of obstruction of the distal superficial femoral or popliteal arteries. *American Journal of Roentgenology*, *150*, 1169–1173.

Takayasu, K., Muramatsu, Y., Moriyama, N., Ohtsu, T. & Catapia, F. C., 1988. Plastic-coated guide wire for hepatic arteriography. *Radiology*, *166*, 545–546.

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*Author for correspondence.

1990, *The British Journal of Radiology*, *63*, 77–78

Case of the month

A pain in the rear

By Richard Suarez, FRCR, *Douglas Morrison, MRCP and †Valerie Suarez, MRCPath

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(*Received July 1989*)

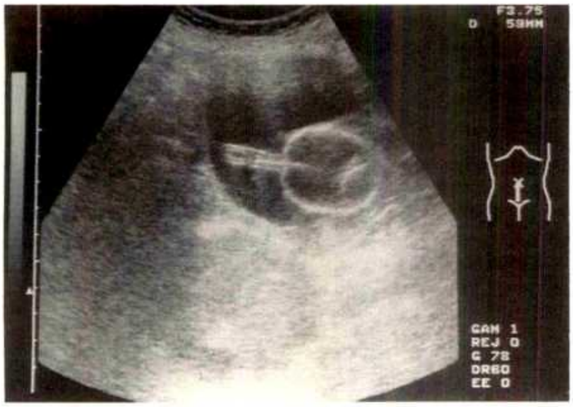

Figure 1. Ultrasound scan of the pelvis.

A 79-year-old, non-insulin-dependent diabetic woman presented with severe pain in the rectum and urgency. A year previously she had been seen because of alternating constipation and diarrhoea. Rectal examination and sigmoidoscopy were normal, but she had a distended bladder and was subsequently catheterized, and this had become permanent. She had had a hysterectomy and bilateral salpingo-oöphorectomy after intracavity radium for carcinoma of the body of the uterus 13 years before.

Examination revealed a lax anus, soft stool, and a soft mass behind the rectum. Sigmoidoscopy was again normal.

Pelvic ultrasound was performed after filling the bladder with saline (Fig. 1). This was followed by a barium enema (Fig. 2). A plain radiograph of the pelvis after barium had cleared is also shown (Fig. 3).

What abnormality is demonstrated on these investigations? What is the differential diagnosis and what other procedures might help in its elucidation?

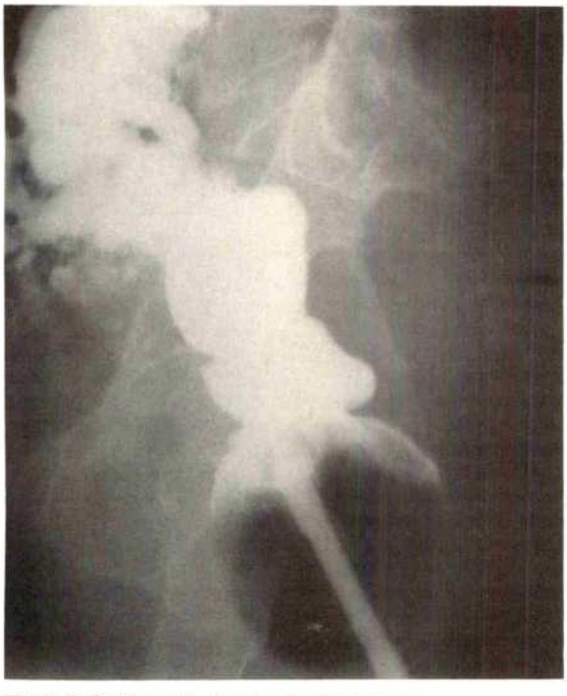

Figure 2. Radiograph showing barium enema.

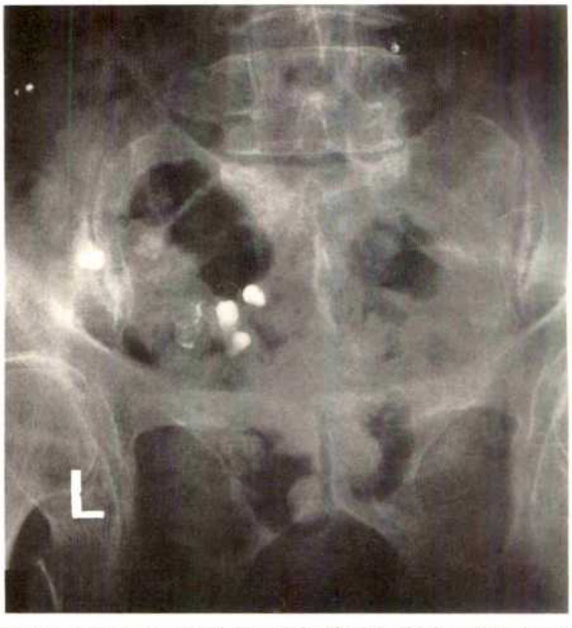

Figure 3. Radiograph of the pelvis after the barium had cleared

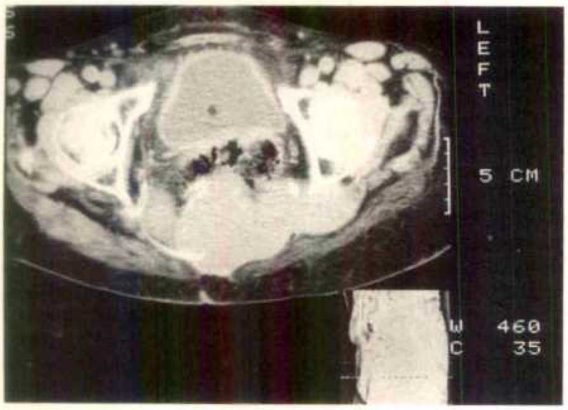

Figure 4. Computed tomography scan demonstrating the extent of the bone destruction and the size of the soft-tissue mass.

The ultrasound scan shows a rounded midline mass lying behind the bladder. This might have been a full rectum, but the initial barium enema radiograph shows the rectum to be displaced anteriorly with an increase in the pre-sacral space. There is a destructive lesion involving the lower sacrum, with irregular, ill-defined margins and containing a few areas of bone or calcification.

A secondary deposit or a radiation-induced sarcoma were considered in view of her previous history. A renal secondary was thought possible from the appearances, but her kidneys were normal on ultrasound examination. A chondrosarcoma might have been expected to contain more calcification. The low midline position of the lesion, her age and its presentation and probable slow growth suggested a chordoma.

A chest radiograph and liver ultrasound examination revealed no other lesions. A computed tomography (CT) scan clearly demonstrated the extent of the bone destruction and the size of the soft-tissue mass (Fig. 4).

The patient subsequently developed a left foot drop, together with reduced power and sensation throughout her left leg.

A fine-needle aspirate (FNA) was performed, and this produced clearish gelatinous material showing on cytology syncytial sheets of malignant cells with marked pleomorphism in a mucoid background and occasional physalliferous cells characteristic of a chordoma.

Palliative radiotherapy produced considerable symptomatic relief.

Discussion

Chordomas are uncommon malignant tumours, accounting for approximately 1% of primary bone tumours and are thought to arise from remnants of the notocord found in the nucleus pulposus and in ectopic rests in vertebral bodies and the sacrum. Some 50% occur in the sacrum; 35% at the skull base, and 15% the spine.

They grow slowly, usually producing symptoms by their mass effect or involvement of adjacent nerves. Distant metastases occur in about 23% of patients with the most common site being lung, followed by skeleton. Less common sites include soft tissues and liver (Smith et al, 1987).

The male to female ratio and age group varies in the two main sites, sacral tumours being most common in older females (O'Neill et al, 1985).

Symptoms are usually non-specific, and the tumours are often symptomatic for more than a year before the diagnosis is made. Pain in the low back or coccygeal region is the most frequent symptom; others include rectal dysfunction (alteration of bowel habit, tenesmus or bleeding) root pain or a mass which may be felt.

On radiological examination, sacrococcygeal chordomas present as a bone tumour with an associated soft-tissue mass, typically the area of bone destruction being midline and involving initially the 4th and 5th sacral segments. As the tumour extends, the entire sacral wings and coccyx may be eroded, the bone edges having an irregular scalloped margin. The soft-tissue mass is usually anterior to the sacrum and extends beyond the area of bone destruction. Calcific densities, mostly consisting of coarse irregular fragments probably representing areas of necrotic bone, are visible on plain radiographs in approximately 40%, but in up to 87% on CT (Smith et al, 1987) Magnetic resonance imaging, with its superior contrast resolution in the demonstration of soft-tissue lesions may well supercede CT as the most sensitive investigation of chordomas (Rosenthal et al, 1985).

Diagnosis can be confirmed by FNA and cytomorphologic findings are characteristic and allow differentiation from other primary and metastatic neoplasms occurring in bone (Finley et al, 1986).

Optimal treatment of sacrococcygeal lesions involves early resection of all tumour or subtotal resection and high-dose radiation in the order of 5000–6000 cGy (Amendola et al, 1986).

References

Amendola, B. E., Amendola, M. A., Oliver, E. & McClatchey, K. D., 1986. Chordoma: role of radiation therapy. *Radiology*, *158*, 839–843.

Finley, J. L., Silverman, J. F., Dabbs, D. J., West, R. L., Dickens, A., Feldman, P. S. & Frable, W. J., 1986. Chordoma: diagnosis by fine-needle aspiration biopsy with histologic, immunocytochemical, and ultrastructure confirmation. *Diagnostic Cytopathology*, *4*, 330–337.

O'Neill, P., Bell, B. A., Miller, J. D., Jacobson, I. & Guthrie, W., 1985. Fifty years of experience with chordomas in southeast Scotland. *Neurosurgery*, *16*, 166–170.

Rosenthal, D. I, Scott, J. A., Mankin, H. J., Wismer, G. L. & Brady, T. J., 1985. Sacrococcygeal chordoma: magnetic resonance imaging and computed tomography. *American Journal of Roentgenology*, *145*, 143–147.

Smith, J., Ludwig, R. L. & Marcove, R. C., 1987. Sacrococcygeal chordoma. *Skeletal Radiology*, *16*, 37–44.

1990, *The British Journal of Radiology*, *63*, 79–80

Short communication

Fractionation sensitivity and the oxygen effect

By J. H. Hendry and *H. D. Thames

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Many normal tissues in natural conditions exhibit slight radiobiological hypoxia (Hendry, 1979). Examples of this in man, which necessitated reductions in dose when the oxygenation status of the tissue was increased, are the skin (van den Brenk et al, 1965), the spinal cord (Coy & Dolman, 1971) and laryngeal cartilage (Churchill-Davidson, 1968; Henk et al, 1977). The expected effect of oxygenation status on fractionation sensitivity has not yet been considered in detail.

Methods and predictions

Fractionation sensitivity can be quantified by the ratio of the parameters α and β in the following equation, which describes the probability (P) of a given level of radiation injury in a tissue following a schedule of doses (x) delivered to a total dose (D).

$$P = e^{-e^{\ln K - \alpha D - \beta x D}}$$

where K is the number of tissue-rescuing units (TRU) (Hendry & Thames, 1986).

It is to be expected that the fractionation sensitivity will depend on the degree of oxygenation of normal tissues, as follows. Decreased levels of oxygenation may occur because of an hypoxic fraction of cells (as in many experimental tumour systems), or because all the target cells are at an almost-constant low level of oxygenation (as probably pertains to most of the normal-tissue systems where hypoxia has been detected) (Hendry, 1979; Hendry et al, 1982; Stewart et al, 1982). With constant low-level oxygenation and with true dose modification (*i.e.* all doses modified by the same factor), α and $\sqrt{\beta}$ would both be higher by the factor OER′ in the oxygenated state (Thames & Rasmussen, 1978), and so the ratio $\alpha/\sqrt{\beta}$ would remain constant. Also, the α/β ratio would then be lowered by the same factor; ln$K$ would remain the same, as there is one end-point common to all irradiation conditions. If oxygen has less of a sensitizing effect at low doses (where α is dominant) than at high doses, as shown for single cells in culture (Palcic & Skarsgard, 1984), then the ratio of the values of α (OER′ at low doses) would be less than the ratio of values of $\sqrt{\beta}$ (OER′ at high doses). When oxygenation status is increased, $\alpha/\sqrt{\beta}$ should decrease and so α/β should decrease more than in the case when $\alpha/\sqrt{\beta}$ is constant. Also, under normal irradiation conditions, if there is induced oxygenation of the slightly hypoxic tissue during fractionation, this may produce an even higher α/β ratio. Thus both of these latter effects could accentuate the decline in α/β ratio with an increase in initial oxygenation status.

These predictions have now been tested by re-analysing data for the incidence of epithelial necrosis in mouse tails (Hendry et al, 1982). The tails were given one, two, four, eight or 16 daily fractions (five per week), while the tails were in air at 27°C, 100% O_2 at 27°C or air at 37°C at the time of irradiation. The effect of these three different conditions, in that order, is to increase the oxygenation status of the target cells (Hendry, 1978).

Results

Direct analysis (Thames et al, 1986) of the results, using a computer program now called $\alpha\beta$est, gave the parameter values listed in Table I in order of increasing oxygenation status. Concomitant increases in α and β were observed as expected. However, the data were not consistent with strict dose modification, because when the oxygenation status was increased, the $\alpha/\sqrt{\beta}$ ratio did not remain constant for all irradiation conditions and the α/β ratio did not decrease in a consistent fashion. Also, the values of ln$K$ for the three sets of data were significantly different ($p < 0.001$), which was unexpected in view of the common end-point used.

Discussion

A possible reason for the observed deviations in α and β from the predictions is greater heterogeneity in the slightly hypoxic conditions (air at 27°C or 100% O_2 at 27°C). This could explain the tendency towards lower values of ln$K$ in these

Table I. Fractionation parameters for mouse tail necrosis

Conditions	ln$K$	10α(Gy^{-1})	100β(Gy^{-2})	$\alpha/\sqrt{\beta}$	α/β(Gy)
27°C, air	5.5 (4.5,6.5)	0.35 (0.27,0.43)	0.23 (0.19,0.27)	1.52	15.3 (13.0,17.6)
27°C, O_2	5.9 (4.2,7.6)	0.37 (0.22,0.51)	0.43 (0.31,0.54)	0.86	8.5 (6.0,10.8)
37°C, air	10.0 (8.1,12.0)	1.26 (1.03,1.49)	0.78 (0.61,0.95)	1.62	16.1 (14.6,18.0)

95% Confidence limits in parentheses.

conditions. If this source of variation reduced α more than it reduced β, this could account for the apparent lack of a consistent decrease in both $\alpha/\sqrt{\beta}$ and α/β with an increase in oxygenation status. Other considerations consistent with this interpretation concern K and Do. A value of 6 for $\ln K$ indicates that $K \simeq 400$ TRU per 2 cm length of irradiated tail (1.3 cm^2 of epidermis). With 1 TRU surviving irradiation, 37% of tails would eventually necrose, which corresponds with about 10 surviving macrocolony-forming cells (CFC) observed per 2 cm length of tail (Hendry, 1984). The resultant deduction of 3×10^3 CFC/cm^2 is lower than reported previously for tail epidermis (6×10^4; Hendry, 1984) and for dorsum (9×10^4, Withers, 1967a, b; 2×10^5, Emery et al, 1970). The value of 1.7×10^5 deduced using $\ln K = 10$ from the 37°C data alone (Table I) is more consistent with the previous values. Also, a Do value can be calculated as $1/(\alpha + 2\beta D)$. At 30 Gy for the 37°C data, Do is ~2.8 Gy. This value is identical to the value of 2.8 Gy reported for single doses only (Hendry, 1984), and similar to the value of 2.7 Gy reported for microcolony-forming cells in tail epidermis irradiated in air at 37°C (Chen & Hendry, 1986). Both these considerations of CFC/cm^2 and Do are consistent with the above argument concerning some degree of heterogeneity among tails in the low-oxygenation conditions.

It is concluded that although there are reasons why the α/β ratio for a tissue should change as a function of oxygenation status, such changes may be masked by different degrees of heterogeneity in sensitivity in different irradiation conditions.

Acknowledgments

We thank Cyndie Smith for assistance with the data analysis, and the Cancer Research Campaign (UK) and the NIC, DHSS (grants CA-29026 and CA-11430) (USA) for financial support.

References

VAN DEN BRENK, H. A. S., KERR, R. C., RICHTER, W. R. & PAPWORTH, M. P., 1965. Enhancement of radiosensitivity of skin of patients by high pressure oxygen. *British Journal of Radiology, 38*, 857–864.

CHEN, F. D. & HENDRY, J. H., 1986. The radiosensitivity of microcolony- and macrocolony-forming cells in mouse tail epidermis. *British Journal of Radiology, 59*, 389–395.

CHURCHILL-DAVIDSON, I., 1968. Long-term effects of hyperbaric oxygen and irradiation on non-neoplastic tissues. *Frontiers in Radiation Therapy and Oncology, 1*, 134–140.

COY, P. & DOLMAN, C. L., 1971. Radiation myelopathy in relation to oxygen level. *British Journal of Radiology, 44*, 705–707.

EMERY, E. W., DENEKAMP, J., BALL, M. M. & FIELD, S. B., 1970. Survival of mouse skin epithelial cells following single and divided doses of X-rays. *Radiation Research, 41*, 450–466.

HENK, J. M., KUNKLER, P. B. & SMITH, C. W., 1977. Radiotherapy and hyperbaric oxygen in head and neck cancer. Final report of the first controlled clinical trial. *Lancet, ii*, 101–103.

HENDRY, J. H., 1978. Radionecrosis of normal tissue: studies on mouse tails. *International Journal of Radiation Biology, 33*, 47–55.

—— 1979. Quantitation of the radiotherapeutic importance of naturally hypoxic normal tissues from collated experiments with rodents using single doses. *International Journal of Radiation Oncology, Biology, Physics, 5*, 971–976.

—— 1984. Correlation of the dose-response relationships for epidermal colony-forming units, skin reactions and healing in the X-irradiated mouse tail. *British Journal of Radiology, 57*, 909–918.

HENDRY, J. H. & THAMES, H. D., 1986. The tissue-rescuing unit. *British Journal of Radiology, 59*, 628–630.

HENDRY, J. H., MOORE, J. V., HODGSON, B. W. & KEENE, J. P., 1982. The constant low oxygen concentration in all the target cells for mouse tail radionecrosis. *Radiation Research, 92*, 172–181.

PALCIC, B. & SKARSGARD, L. D., 1984. Reduced oxygen enhancement ratio at low doses of ionising radiation. *Radiation Research, 100*, 328–329.

STEWART, F. A., DENEKAMP, J. & RANDHAWA, V. S., 1982. Skin sensitization by misonidazole: a demonstration of uniform mild hypoxia. *British Journal of Cancer, 45*, 869–877.

THAMES, H. D. & RASMUSSEN, S. L., 1978. A test for dose-modifying factors. *Radiation Research, 76*, 308–324.

THAMES, H. D., ROZELL, M. E., TUCKER, S. L., ANG, K. K., FISHER, D. R. & TRAVIS, E. L., 1986. Direct analysis of quantal radiation response data. *International Journal of Radiation Biology, 49*, 999–1009.

WITHERS, H. R., 1967a. Recovery and repopulation *in vivo* by mouse skin epithelial cells during fractionated irradiation. *Radiation Research, 32*, 227–239.

—— 1967b. The effect of oxygen and anaesthesia on radiosensitivity *in vivo* of epithelial cells of mouse skin. *British Journal of Radiology, 40*, 335–343.

1990, *The British Journal of Radiology*, *63*, 81–82

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Chemical protectors: their potential application against occupational radiation hazards

THE EDITOR—SIR,

The last two decades have seen a tremendous effort to find suitable chemicals that can be used for normal-tissue protection in tumour radiotherapy. The most promising compound so far is the synthetic phosphorothioate derivative of cysteamine (WR-2721), studied extensively for its protective effect in mammals and man (Yuhas, 1980). The initial enthusiasm was dampened by the discovery that repeated injections of this drug in man produced undesirable toxic side effects (Utley et al, 1976; Turrisi et al, 1983), as well as by the controversy regarding the preferential protection of normal tissues by the drug (Denekamp et al, 1983). According to Denekamp and Rojas (1987), WR-2721 is unlikely to become a widely used adjunct to conventional radiotherapy.

Another drug, 2-mercaptopropionylglycine (MPG), caught the attention of scientists because of its non-toxic nature and its effectiveness after oral administration, but its low level of protection makes it a less attractive candidate for use in clinical radiotherapy (Sugahara et al, 1970). Many recent studies have therefore concentrated on methods to reduce the toxicity of WR-2721 and on finding alternative drugs which are more potent and less toxic. However, no suitable chemical protector is available so far that can be routinely used in clinical practice.

One area where SH protectors can be of practical application appears to be in the field of health physics, where workers are exposed to the risk of occupational radiation hazards. The radiation workers receive a level of exposure higher than background in the course of their work, and sometimes minor accidents or work related to maintenance and repair of nuclear facilities will increase the exposure levels, with a consequent increase in the risk to the person. The main effect from such exposure is a change in chromosomes which can lead to later complications, including cancer and genetic effects, which will be manifested in subsequent generatioins (UNSCEAR, 1982). Pregnant women face a higher risk because of the high susceptibility of developing embryos to very small doses of radiation, amounting to only a few cGy.

Experiments on mice exposed to sublethal doses of γ radiation ranging from 50 cGy to 600 cGy, using WR-2721 below the maximum tolerated dose and MPG at the optimal dose, have shown that both drugs are effective in reducing radiation-induced chromosomal aberrations in the bone marrow cells, and WR-2721 is better in this respect (Gupta and Uma Devi, 1986). Furthermore, it was also seen that a dose of WR-2721 (150 mg/kg) as low as about 25% of the maximum tolerated dose (MTD) can give very good protection against chromosome damage with little drug toxicity when followed by a post-irradiation injection of an optimal dose (20 mg/kg) of MPG (Thomas and Uma Devi, 1987) (Table I). Further studies have shown that even 50 mg/kg of WR-2721, when followed by 20 mg/kg of MPG, significantly reduced the radiation-induced micronuclei in mouse bone marrow ($p<0.001$) (Prasanna and Uma Devi, 1989), with no accompanying drug toxicity. An earlier report has shown that MPG given to pregnant mice before low-dose γ exposure could protect against some of the radiation-induced changes in the offspring (Dev et al, 1981).

Table I. Protective effect of the drugs on the bone marrow chromosomes of Swiss albino mice whole body exposed to 4.5 Gy γ radiation, observed on Day 1 post-irradiation

Treatment[a]	Drug dose (mg/kg)	Normal metaphases (%)
Control		44.17±0.92
WR-2721	300	77.66±1.11 $p<0.001$
	150	69.33±1.17 $p<0.001$
MPG	20	58.50±0.86 $p<0.001$
WR-2721+MPG	150+20	76.83±1.54 $p<0.001$

These findings indicate that, even though the application of thiol protectors in radiotherapy is still a long way off, these drugs could be useful for the protection of radiation workers against the risks from unavoidable low level irradiation and planned exposures.

Yours, etc.
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References

DENEKAMP, J., ROJAS, A. & STEWART, F. A., 1983. Is radioprotection by WR-2721 restricted to normal tissue? In *Radioprotectors and Anticarcinogens*, ed. by O. F. Nygaard and M. G. Simic (Academic Press, New York), pp. 655–679.

DENEKAMP, J. & ROJAS, A., 1987. Radioprotection *in vivo*: cellular heterogeneity and fractionation. In *Anticarcinogenesis and Radiation Protection*, ed. by P. A. Cerutti, O. F., Nygaard and M. G. Simic (Plenum Press, New York), pp. 421–430.

DEV, P. K., GUPTA, S. M., GOYAL, P. K., MEHTA, G. & PAREEK, B. P., 1981. Radioprotective effect of MPG (2-mercaptopropionylglycine) on the post-natal growth of mice irradiated *in utero*. *Strahlentherapie*, *157*, 553–555.

GUPTA, R. & UMA DEVI, P., 1986. Protection of mouse chromosomes against whole body γ irradiation by SH compounds. *British Journal of Radiology*, *59*, 625–627.

PRASANNA, P. G. S. & UMA DEVI, P., 1989. Influence of drug combination on the radioprotective and toxic effects of S-2-(3-aminopropylamino) ethyl phosphorothioic acid (WR-2721) on mouse bone marrow. In *Proceedings of the First Afro-Asia Oceania Congress of Anatomists, New Delhi, August 29–September 3, 1988* (in press).

SUGAHARA, T., TANAKA, Y., NAGATA, H., TANAKA, T. & KANO, E., 1970. Radiation protection by 2-mercaptopropionylglycine. In *Proceedings of the International Symposium on Thiola* (Santen Pharmaceutical Co., Japan), pp. 262–272.

THOMAS, B. & UMA DEVI, P., 1987. Chromosome protection by WR-2721 and MPG: single and combination treatments. *Strahlentherapie*, *163*, 807–810.

Turrisi, A. T., Kligerman, M. M., Glover, D. J., Glick, J. H., Norfleet, L. & Gramkowski, M., 1983. Experience with phase I trials of WR-2721 preceding radiation therapy. In *Radioprotectors and Anticarcinogens*, ed. by O. F. Nygaard and M. G. Simic (Academic Press, New York), pp. 681–694.

UNSCEAR, 1982. Ionizing radiation: sources and biological effects. *Report to the General Assembly, E82, IX8* (United Nations Publication, New York).

Utley, J. F., Phillips, T. L. & Kane, L. J., 1976. Protection of normal tissues by WR-2721 during fractionated irradiation. *International Journal of Radiation Oncology, Biology, Physics, 1*, 699–703.

Yuhas, J. M., 1980. On the potential application of radioprotective drugs in solid tumor therapy. In *Radiation-Drug Interactions in the Treatment of Cancer*, ed. by G. H. Sokol and R. P. Maickel (John Wiley & Sons, Englewood Cliffs, NJ), pp. 113–135.

Isoeffective doses

The Editor—Sir,

The interesting letter of Bentzen and Thames (1989) contains a small, but not entirely trivial, error: 51 Gy in 12 fractions should be isoeffective with 37.96 Gy in six fractions, not 37.4 Gy as stated. The use of the corrected figure strengthens the argument in Dr Bates' reply.

Yours, etc.,
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(*Authors' reply*)

The Editor—Sir,

We thank Dr Scott for correcting our calculation (Bentzen & Thames, 1989) of the dose in six fractions being isoeffective with 51 Gy in 12 fractions. It was not our intention to question Dr Bates' result obtained by using an α/β at 2 Gy but rather to make the point that the uncertainty in our current knowledge of α/β for subcutaneous fibrosis further complicates the interpretation of the results of the St Thomas' trial. Our best current estimate of α/β for subcutaneous fibrosis is 1.9 Gy with 95% confidence limits of 0.8 and 3.0 Gy (Bentzen et al, 1989). This produces an isoeffect dose in six fractions at 38.05 Gy with 95% confidence limits of 36.98 and 38.95 Gy. While the upper limit would seem to be an overestimate of the isoeffect dose given in six fractions, the lower limit is not necessarily so.

The point we wanted to make in our letter is that the linear-quadratic (LQ) model with an α/β at about 2 Gy predicts a lower incidence of subcutaneous fibrosis after 35 Gy in six fractions than after 51 Gy in 12 fractions—exactly what was observed in the St Thomas' trial. We do agree with Dr Bates that the LQ model should be used with great care in the clinic. However, we maintain that with our current knowledge the result of the St Thomas' trial does not conflict with the LQ model predictions.

Yours, etc.,
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References

Bentzen, S. M. & Thames, H. D., 1989. Are the results of the St Thomas' trial of post-mastectomy radiotherapy inconsistent with the predictions from the linear-quadratic model? *British Journal of Radiology, 62*, 633–634.

Bentzen, S. M., Thames, H. D. & Overgaard, M., 1989. Latent-time estimation for late cutaneous and subcutaneous radiation reactions in a single-follow-up clinical study. *Radiotherapy and Oncology, 15*, 267–274.

Atlanto-axial rotary fixation

The Editor—Sir,

We read with interest the paper by Moss et al (1989) on the diagnosis of atlanto-axial rotary fixation by functional computed tomography (CT). We have recently seen two young adults with resistant torticollis but no neurological symptoms following minor neck trauma. Routine antero-posterior, open-mouth, upper cervical spine radiographs revealed some asymmetry of C1 on C2, and subsequent CT of both patients confirmed the presence of atlanto-axial rotary fixation. Each patient made an uneventful recovery with conservative management.

We agree with Moss et al (1989) that unexplained persistent torticollis, particularly in children, should not be ignored. Early consideration of the possible presence of atlanto-axial rotary fixation and assessment by functional CT is strongly recommended.

Yours, etc.,
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Reference

Moss, J. G., Sellar, R. J. & Bradnock, B., 1989. Atlanto-axial rotary-fixation: diagnosis by functional computed tomography. *British Journal of Radiology, 62*, 755–758.

Corrigendum

British Journal of Radiology, November 1989.

In the letter from T. Conere et al (An interesting radiation protection finding around a linear accelerator, *BJR, 62*, 1033) the sentence in the third paragraph, "For nominal beam qualities of 6 MV, the magnitude of radiation scatter laterally in $\text{cGy mA}^{-1}\text{min}^{-1}$ differs by a factor of ~ 2 (Karzmak & Pering, 1973)" should read, "For nominal beam qualities of 6 and 16 MV, the magnitude of radiation scatter laterally in $\text{cGy mA}^{-1}\text{min}^{-1}$ differs by a factor of ~ 2 (Karzmak & Pering, 1973)."

1990, *The British Journal of Radiology*, *63*, 83–86

Book reviews

MRI Atlas of the Abdomen. By Ralph Weissleder and David D. Stark, pp. viii + 200, 1989 (Martin Dunitz, London), £65.00.
ISBN 0–948269–45–6

This book succeeds very well in its aims to provide up-to-date technical information and to demonstrate the clinical applications of abdominal MRI. The illustrations are of high standard although the same illustration may appear more than once to explain a different point. They are accompanied by informative legends that are easy to understand and when necessary, diagrams and simple graphs are used.

The first chapter discusses MR techniques with special reference to the abdomen. Although a basic knowledge is assumed, pulse sequences are explained with simple diagrams to aid the reader less familiar with MRI. The factors influencing image quality and contrast are well explained and artefact production is mentioned.

The following chapters discuss the liver, biliary system, spleen, pancreas, alimentary tract, kidneys and vasculature. There is a brief introductory text but more information is found in the legends. The normal anatomy is demonstrated by the most commonly used pulse sequences (this atlas has examples obtained mainly with a medium-field-strength magnet) and the pathology of each system is then discussed and illustrated. The use of contrast agents, if appropriate, is mentioned within each chapter. The most extensive section is that on the liver, which reflects the authors' interests and the current state of research.

I found the atlas easy to read and quite interesting. It has, however, a very limited audience in this country. Its price (£65.00) is reasonable for an atlas, but unless departments have access to a machine carrying out abdominal imaging, it would be difficult to justify its purchase.

JULIE OLLIFF

The Place of Panoramic Tomography in Dental Radiography — What Radiographers Should Know About Dentistry. By Josephine Semple and Daphne Gibb, pp. 59, 1988 (College of Radiographers, London), £2.50.
ISBN 1–871101–00–X

The main authors of this A4 format book are two experienced radiographers working in collaboration with several consultant dental surgeons, a representative of Siemens Ltd, and the College of Radiographers. The slim volume is a collection of articles previously published in *Radiography*, together with a supplement, and is intended to provide general radiographers with not only an insight into dentistry, so that the value of various radiographic techniques becomes apparent, but also a resumé of the shortcomings of some of these techniques.

The first chapter is divided into two to deal initially with a history of the development of dental panoramic tomography, the principles and practice of the technique and radiation doses. There are also illustrations of normal radiographic anatomy and the results of faulty patient positioning. The second half outlines the shortcomings of the panoramic technique with particular reference to width of focal trough, production of secondary shadows, image overlap and superimposition. This chapter, written by the radiographers, is a good introduction but a comparison of magnified illustrations of high-quality dental radiographs with minified illustrations of tomograms is an overstatement of a case. The presentation of tables of doses to areas on the head without putting them into the perspective of everyday risks is unhelpful, as is the comparison of these doses from an elderly OPG 3 machine with those from other unqualified dental X-ray equipment. However, the introduction is comprehensive and is followed by the four generally clear, succinct and helpful chapters written predominantly by the dental surgeons. Because of the multiauthorship there is a little repetition, but the level of the discussion is just right for the proposed readership. There are a few examples of spelling errors and transposition of illustrations but these faults do not detract from the message that whilst a dental panoramic tomogram provides an extremely useful overall view of the teeth and jaws, it does have its limitations and these can and must be overcome by the judicious use of either alternative or additional examinations. One of these examinations is described in the chapter that discusses occlusal radiography and submandibular salivary gland calculi. The well illustrated description is a welcome one, which will enable interested readers to add to their armamentarium.

The last multipage chapter contains a lucid account of the Zonarc programmed tomography unit. This is derived from manufacturer's literature and illustrates a more recent application of panoramic tomographic techniques to the structures of the head and neck. There are only a few such units in the UK and most radiographers will never use one, but the chapter does demonstrate that panoramic tomographic technique is not confined to that of the OPG and is not stagnant. Radiation dosage details are given but in the same form as in the first chapter.

The final page is a brief, staccato synopsis of radiation protection in dentistry. The contents are derived from International Commission on Radiological Protection and other publications and include an important comment on the relatively limited value of protective aprons in dentistry. There is a glaring error of omission of the word "not" from the sentence "Dental radiography should be routine at every visit but should be based upon definite indications."

This book is a useful contribution to the literature. It is inevitably slightly dated by its reference to equipment used at a dental hospital that is now closed, but its contents will interest and help its intended readership. One could easily comment adversely on illustrations of certain of the radiographic techniques but the authors do state that they are not publishing a technique text. I doubt if individuals will purchase this book but it would certainly not be out of place in the library of a department that does not specialize in dental radiography.

J. B. HUTTON

Clinical Application of Cardiac Digital Angiography. Ed. by G. B. John Mancini, pp. xii + 324, 1988 (Raven Press, New York), $99.00.
ISBN 0–88167–361–7

Although digital vascular imaging has been with us for several years, the cardiac applications of this technique have been limited by the need for high frame rates required for cine cardiac imaging. In the past only tape based systems such as the Siemens angiotron have been able to give subtracted images at 25 or 50 frames a second. These systems suffer from the disadvantage of limited post processing and analytical facilities. As newer systems become available there will be an increased interest in cardiac applications of digital imaging.

This book is a collection of papers by different authors with the aim as outlined in the introduction of "bringing together the work of many of the investigators throughout the world who initiated and continue to advance the field of cardiac digital angiography". There are 19 chapters, and 24 contributing authors from 14 centres predominantly in the USA but with contributions from Switzerland, West Germany and Australia. The chapters were obviously written independently as some of the material is repetitive; however, the standard of contribution is high. Most of the chapters take the form of extended scientific papers with a large proportion of original data combined with extensive literature reviews on each topic. The initial chapters deal with physics, instrumentation, archiving and image processing. These chapters are heavy going. However, there is a good discussion on the problems of obtaining a subtracted image for the moving heart. In the archiving chapter there is a section on the cost-effectiveness of digital image storage showing how non-cardiac digital imaging has risen to 30% of total imaging in the authors' centre (Kansas Medical Centre). Automated edge detection is dealt with very well. Apart from three more general chapters on parametric imaging, intravenous versus intra-arterial injection and an overview chapter on the role of digital subtraction angiography in congenital and valvular heart disease, the rest of the book deals with specific cardiac physiological parameters and how digital imaging can measure them. Comparison with other techniques tends to be downplayed, as do the technical difficulties, and many of the practical problems are not clearly addressed. The standard of illustrations is variable; the illustrations are used to accompany the data rather than to provide a guide to the appearance of digital subtraction images in cardiac disease.

The major deficiency is in dealing with imaging of congenital heart disease. In the UK there are very enthusiastic proponents of digital subtraction using small injections of contrast medium and this is one of the main clinical uses of cardiac digital subtraction at this time; however, congenital disease accounts for only two to three of a total of 334 pages in the book.

The book is certainly not light bedtime reading but with its extensive bibliography will be essential reading for anyone researching into this area. It will also be useful to have it on the shelf in any cardiac angiographic laboratory that has digital imaging. It is of little use as a training manual or as an introductory text to the subject.

MICHAEL R. REES

Atlas of Nuclear Medicine. Ed. by D. van Nostrand and S. Baum, pp. xiv + 428, 1988 (Lippincott, Philadelphia), £55.00. ISBN 0-397-50789-5

In the current spate of medical publications, one approaches an "atlas" with a cynical feeling of paying heavily for a minor increase in real knowledge. This atlas, however, does represent a useful volume. Its success lies in the choice of subject matter involving selected, often lesser used, diagnostic tests, which are well described and illustrated. Each chapter briefly outlines the literature, the technique and clinical indications. The majority of these introductions are fairly substantial and well referenced reviews. This is followed by a series of illustrative cases. Subjects range from oesophageal transit studies to paediatric radionuclide lymphology. They are all, in the view of the editors, procedures that are dealt with inadequately in larger texts, but do not merit a book or a monograph of their own.

The volume opens with a section on oesophageal transit studies. The use of a radioactive tracer to record oesophageal function has the same advantages as its use for ureteric reflux: events can be recorded *in toto* and processed in a way that is difficult to achieve with cine recordings. Abnormalities of the oesophagus and pharynx, although common, particularly in the elderly, are not well dealt with in many radiology departments. The contribution of radionuclide studies to the tongue and pharynx may be pathology-limited by image resolution, but abnormalities of peristalsis and emptying in the oesophagus such as occur with scleroderma, myotonia, diverticula and reverse peristalsis with reflux can all be clearly recorded and analysed. As with many procedures in nuclear medicine, this technique is only useful if linked with radiology, but any centre with a particular interest would do well to combine these two approaches.

Two chapters are devoted to adrenal imaging or, more correctly, imaging of the adrenal cortex, medulla and related tissues. They are authoritative accounts of a rather complex area but rather poorly illustrated because of the almost exclusive use of iodine 131 rather than iodine 123. The use of steroid suppression of the adrenals when imaging Conn's syndrome is well discussed and illustrated (a problem not easily resolved from standard texts). The section on imaging with methyl iodo benzyl guanidine (MIBG) makes it clear that iodine 131 is not a reliable tracer and that iodine 123 is the agent of choice.

There is a very useful chapter on renal studies in the transplant kidney. This is based on both imaging and indices derived from DTPA and hippuran. Renal blood flow is assessed from rapid sequential imaging, from the rate of increase of tracer over the kidney and as a figure for effective renal plasma flow derived from a single blood sample. The data unfortunately do not deal with current difficulty — that of differentiating rejection from cyclosporin toxicity, and this is a gap in an otherwise excellent chapter. A variety of other topics are covered: parathyroid scintigraphy (which is not quite as good as some of the literature would suggest), iodine 131 imaging of the neck and chest, testicular imaging, and the use of In-111 labelled leukocytes. The standard of illustration is high with sensible explanatory legends. All this constitutes reasonable value for money (£55) and one might wonder if there is to be a sequel.

J. P. LAVENDER

Atlas of Anatomic Correlation in CT and MRI. By Paul Gerhardt and Walter Frommnold, pp. viii + 173, 1988 (Georg Thieme Verlag, Stuttgart), DM 480.
ISBN 3-13-662001-1 (Stuttgart)
0-86577-227-4 (New York)

This is a particularly large and impressive tome, which deals with normal sectional anatomy in both CT and MRI. The authors have attempted to create a reference atlas that correlates axial, sagittal and coronal anatomical sections of the head and body with computerized and MR tomographic sections. In this respect they have succeeded admirably. The book is sensibly divided into anatomical regions — the head, neck and thorax, abdomen and pelvis with an initial chapter covering whole body coronal and sagittal sections.

The atlas is beautifully presented and illustrated. The anatomical drawings, prepared by Karl Herzog, are of the highest quality; they are clear, comprehensive, anatomically correct and well annotated. In the head chapter, photographs of sectioned cadaveric brain supplement the drawings with good effect. The CT and MR images that are presented are also of a high standard and generally correlate well with the illustrations. Annotation is again accurate and clear. Some of the inversion–recovery features of the brain are of poor resolution but all the salient sagittal CT "Lego brick" reconstructions of the brain add little to the detailed MR images.

The high price and large size of this atlas suggests that it is primarily intended as a desktop reference manual and, in general, it is well suited to this use. Given the still low availability of MRI in this country, the overall balance of CT and MRI in the atlas is about right. While CT is covered comprehensively, there are some surprising omissions in the field of MR. The atlas does not cover anatomical detail of the musculoskeletal system, surely one of the most relevant areas to the radiologist practising MRI. Some T_2-weighted images would have been of value as anatomy can appear quite distorted in this pulse sequence.

To summarize, this text can be recommended for purchase as a general reference atlas for a CT or MR department, where it is likely to be well used, although it should not be expected to cover all anatomical aspects relevant to these imaging techniques.

H. G. Lewis-Jones
D. I. Lewis-Jones

Basic Physics for Medical Imaging. By Edwin Aird, pp. viii + 262, 1988 (Heinemann, London), £17.50.
ISBN 0-433-00044-9

This small textbook is aimed primarily at trainees in radiology preparing for the Part I FRCR examination, the author being an examiner in the therapy section. The best person to assess this type of manuscript is a registrar who has just been through this experience and so the following is a combined review. The book begins with a chapter on basic physics and electronics. This constitutes a useful revision since it will have been several years since most of the readers will have studied these subjects and they are topics that many other textbooks do not include. In the following chapter on radiation physics, the first of several weaknesses becomes apparent. Terms such as "dose" and "exposure" are inadequately explained and words such as "absorption edge" and "forbidden band" appear without explanation. The half-page of text devoted to mammography is too little for such an important and topical subject. The chapter on nuclear medicine contains rather misleading statements as demonstrated by the suggestion that lung scans are useful in the diagnosis of pulmonary tuberculosis, lung cancer and mitral stenosis. They may have a role to play in these diverse conditions but hardly an important one. Whilst most radiology trainees will readily reject this information, others reading this book may not be so well informed. The statement on page 155 declaring that "a definite diagnosis of a viable multiple pregnancy is not possible until after the first trimester" is interesting to say the least! The final chapter on radiation protection is merely a brief introduction to the subject and provides insufficient information for the Part I FRCR examination.

One of us has been an examiner for the Part I diagnostic board for the last 4 years, and this text does not have enough depth or quality to recommend it. There are other, similarly priced works designed for the Part I examination that offer better value. We are very concerned about the medical aspects contained in this book and we hope the input will be substantially upgraded if a second edition is forthcoming. The physics content is not detailed enough for a trainee radiologist to expect to pass the Part I examination without substantial further study.

J. Weir
J. Reynolds

Practical Ultrasound. Ed. by R. A. Lerski, pp. xii + 243, 1988 (IRL Press, Oxford), £25.00, US$50.00 (softcover); £38.00, US$76.00 (hardcover).
ISBN 1-85221-157-1 (softcover)
1-85221-068-0 (hardcover)

This relatively compact book, edited by R. A. Lerski, consists of 15 chapters written by different authors and covers the physics and many medical applications of diagnostic ultrasound.

The first five chapters are devoted to basic physics including chapters on Doppler and performance checks. The information and diagrams are clearly presented and subheadings within chapters are clearly labelled in bold print. Each of these chapters is between 10 and 15 pages in length. However, the one concerning performance checks runs to nearly 30 pages and I feel that this is a little long when considered in relation to the length allowed for other chapters.

There are 14 chapters devoted to medical applications, including obstetrics, gynaecology and abdominal scanning. Editorial constraints would appear to have made some of the sections within these chapters rather short and the trainee would need to make use of the comprehensive and, in the main, up-to-date reference and recommendations for further reading to be found at the end of each chapter. Chapters on echocardiography, ocular scanning and safety aspects, as well as interventional ultrasound, all within a total of 250 pages, demonstrate how the editor has, in the main, succeeded in fitting a quart into a pint pot. The illustrations in the medical applications section are clear, well labelled and, for the most part, up to date.

This book is an ideal introduction for trainee sonographers and sonologists. In softback form it represents excellent value for money. A hardback version is also available for library and departmental purchase.

G. Lamb

Essential Chest Radiology. By J. B. Cookson and D. B. L. Finlay, pp. vi + 151, 1988 (Heinemann, London), £12.50.
ISBN 0-433-00041-4

This is a pocket-sized book of 151 pages written in the style of an atlas of chest radiographs with clinical correlation. There are 10 chapters covering radiographic technique, normal anatomy, pulmonary shadows, chronic obstructive lung disease, pleura chest wall and diaphragm, the hila, the mediastinum, the heart and special techniques.

The stated aim of this book is to provide a concise atlas with clinical correlation suitable for the senior medical student and junior doctor. In addition the preface suggests that MRCP and FRCR candidates would find the book helpful.

The quality of the illustrations, both the radiographs and line drawings, is of a high standard. The points made in the text and legends are all clearly identifiable on the relevant plate, and free use of arrows helps the novice to be sure of the lesion being discussed. The text is clearly and well written. All the more common pulmonary and mediastinal pathologies are covered, albeit in a superficial fashion. Nevertheless, the degree of discussion is sufficient to provide a useful synopsis for the non-expert, and to draw attention to the more usual pitfalls that face the junior doctor. Much less emphasis is placed on the heart, with just four radiographs in that chapter. Coverage of special techniques is also sketchy, but in terms of the intended audience is probably adequate.

Inevitably there are minor spelling errors, and one rather more serious printing error with mislabelling of the upper and lower lobe posterior segments of the right lung. A little more editorial attention to the layout of Figs 2.3 a, b and c could have reduced the constant flicking back and forth over a page when comparing the frontal and lateral projections of pulmonary lobar anatomy. The bibliography has only two references, one from 1973 and the other from 1978. Whilst both books are classics, they would provide daunting reading for doctors without a specialist interest in chest radiology or chest medicine. In general terms, the book reads well, and can be read in one sitting.

At this price the book is excellent value, it admirably fulfills its aims and is within the reach of senior students both in terms of cost and content. There is just enough detail to make this book useful for the non-specialist sitting membership or surgical fellowship. There is insufficient material to sustain this text as a major reference for the radiologist sitting FRCR; however, it would be useful as a quick guide in moments of self doubt just before the film viewing viva!

In conclusion, this is a welcome little book, which is to be recommended for its intended audience of non-specialist junior doctors and final-year medical students.

G. J. HUNTER

Roentgen Signs in Diagnostic Imaging, 2nd edn, Vol. 4: The Chest. By I. Meschan (with assistance of R. M. Farrer-Meschan), pp. xxx + 1038, 1987 (W. B. Saunders, Philadelphia), £72.75.
ISBN 0-7216-6298-6

This is the fourth volume of a completely rewritten version of *Analysis of Roentgen Signs in General Radiology* (1973). It replaces the previous Volume 2 and has grown considerably, from about 500 to 1000 pages. It now has just over 1000 figures and about 1300 references, the most recent being 1985. The emphasis is on conventional radiology and computed tomography and these represent the bulk of the illustrations with a little MR, including a short appendix on MR in congenital heart disease. There are 13 chapters with I. Meschan as an author in all but one and five other contributors to seven chapters (R. E. Bechtold, M. L. Bertrand, B L. Carter, A. G. Formanek and R. D. Pugatch).

The 13 chapters cover the chest (wall, pleura, diaphragm, lungs, air passages and mediastinum) and congenital and acquired diseases of the heart and great vessels with new ones on the breast, larynx and the paediatric chest. Some chapters are organized around an anatomical structure, *e.g.* larynx, and others around a radiological finding, *e.g.* nodular lesions of the lung, parenchyma. Where appropriate, chapters consider basic and radiological anatomy, examination techniques, radiological signs and differential diagnosis. The bulk of the text is concerned with the radiological signs and these are explained and amplified with numerous radiographic illustrations and the familiar "Meschan" line drawings, many of which have been transferred from the previous volume. In discussing the differential diagnosis of each sign, the opportunity is taken to discuss various diseases and disorders.

Although it is not clearly stated, this volume is pitched at the level of a senior trainee in radiology and it might also provide useful reference once training is complete. I personally did not find the book easy to read and in part I think this is due to the authors' attempt to communicate an enormous number of facts. In addition, facts are not always presented in a logical and orderly fashion and their relative importance is often not indicated. There is no doubt that the main thrust of the book is concerned with signs but at the same time, in the differential diagnoses that relate to the signs, disorders and diseases are discussed. Since the layout of the book is dictated largely by signs, consideration of various diseases is often fragmented. Many of these discussions, presumably for reasons of space, are very abbreviated. For example, sarcoidosis is covered in about three pages of text and this leads to a disparity in the depth of discussions relating to signs on the one hand and disorders on the other. It also means that the book is not detailed enough to use as a source of reference for lung diseases and disorders. In general, the points to be made in photographic illustrations come across, but I find some of the line diagrams irritating, *i.e.* those transferred from the earlier volume that are complicated by excess detail and shadowing. Some figure numbers on illustrations and the text do not match up.

This is a book that contains a wealth of information, particularly concerning the plain radiographic and CT signs of chest and heart disease. I personally felt, however, that the author did not succeed in the task of making these facts easy to assimilate.

A. G. WILSON

1990, *The British Journal of Radiology*, *63*, 87–88

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References

BCRU, 1980. Quantities for reporting the calibration of therapy-level dosemeters in photon beams. *British Journal of Radiology*, *53*, 917-918.

——— 1982a. Use of air kerma for photon dosimetry in air. *British Journal of Radiology*, *55*, 375-376.

——— 1982b. SI units for radiation protection—an interim measure. *British Journal of Radiology*, *55*, 376-377.

BIOLOGICAL COUNCIL, 1987. *Guidelines on the Use of Living Animals in Scientific Investigations, 2nd edn.* Obtainable from Mrs. B. Cavilla, c/o Institute of Biology, 20 Queensberry Place, London SW7 2DX.

BIR WORKING PARTY ON SI UNITS, 1981. Conversion to SI Units in radiology, *British Journal of Radiology*, *54*, 377-380.

INSTITUTE OF PHYSICS, 1983. *Notes for Authors.* Obtainable from Institute of Physics Publications Dept., Techno House, Redcliffe Way, Bristol BS1 6NX.

JENNINGS, W. A., 1981. How much do you know about quantities and units? *British Journal of Radiology*, *54*, 381-383.

NATIONAL PHYSICAL LABORATORY, 1987. *The International System of Units*. (SI). Ed. by D. T. Goldman and R. J. Bell (5th Edition), Her Majesty's Stationery Office, London (£4.95).

THE ROYAL SOCIETY OF MEDICINE, 1988. *Units, Symbols and Abbreviations: a Guide for Biological and Medical Editors and Authors* (£5.00). RSM, 1 Wimpole Street, London W1M 8AE.

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Review article

Computers in radiology departments

By G. R. Sutherland, FRCP(Edin), FRCP(Glas), FRCR

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It is only a few years since computers were essentially regarded by the public as complicated machines used only by banks, major industrial concerns and research establishments. But the situation is changing rapidly to one where in every household the computer will sit alongside the video tape recorder and the television set. Every schoolchild is now taught how to use computers and elementary keyboard operation skills. They are pervasive throughout our society. A tremendous development of their use by small businesses has occurred where this would not have been considered cost effective only a few years ago. However, it is only with the publication of the "White Paper" on the most recent reorganization of the Health Service that the importance of introducing computers for information management has ultimately been recognized as central to the effective management of the Health Service. It appears that the financial implications of such developments have also been accepted.

Radiologists in this country have been trying to acquire computing systems for their departments for many years now, and many have been effective, but there is still a large core of individuals who remain to be convinced of the effectiveness of such systems in the running of their departments, and it is with the objective of convincing them of the applications and usefulness of computer systems that this article has been written (Sutherland, 1983).

What is a computer system?

Unfortunately, like many specialties, the computer world is full of jargon that the uninitiated find difficult to understand. Fortunately much of this is of no particular significance to the end user, as few, if any of them, are now required to be programmers. Indeed modern computer systems can be treated very much as the "black boxes" that some years ago we were told that they could never be (Bradburn et al, 1982; Asbury, 1983a). This is well demonstrated by the computer-based typewriters that are so widely available. The typist knows nothing of the computer system that controls the display and so allows her to check her spelling before the phrase is printed. She uses the memory keys storing text, and formulates standard letters without even recognizing that she is using a word-processing package. At the other end of the scale, there are the massive so-called main-frame computers capable of handling hundreds of thousands of tasks simultaneously. In between, the smallest machines are called microcomputers, which are the most familiar, and the middle-sized or minicomputers, which form the majority of computers used in normal commercial and industrial environments. It used to be easier to define these different groups of computers, but with rapid developments in technology the differences are becoming less distinct with powerful modern microcomputers outdistancing even middle range minicomputers of yesteryear.

Hardware

The "hardware" of a computer system comprises the electronic equipment of the system consisting of the computer itself, which processes the information, a means of storing data—usually a form of magnetic or even optical disc system and a video display unit (VDU) with a keyboard, which allows the operator to communicate with the machine and the information it contains and to see the outcome of the computer's activity. A printer is required if a permanent record of the output is needed (Asbury, 1983a, b).

Software

The "software" represents the program of instructions given to the computer to carry out the task or tasks required. Such programs are generally stored on some form of magnetic disc connected to the system and read into the computer memory; they are then available to carry out the instructions given by the user (Asbury, 1983c, d).

Programs may be purchased as a package, for example for a small business user, which undertakes the maintenace of a list of clients, provides an accounting system and a means of sending out bills or accounts, a supplies or stores facility and perhaps a means of doing a financial projection for the company. Word-processing facilities for the formulation of letters, reports etc. are commonly part of such a package of programs.

Although such programs are designed for small businesses, the functions are usually sufficiently general that they may be applied in a wide range of different office environments, and indeed, many are being used in radiology departments quite successfully. If more specific functions are required, it may be necessary to write a particular program, although often the suppliers of software may be able to adapt an existing program to suit. With earlier software systems this was often time-consuming and therefore expensive, but with modern computer languages, the so-called 4th generation languages (4 GL), this is no longer the case. Instead of having to alter large tracts of symbolic language, the adaptation of modern programs is done, essentially, in plain English.

The other characteristic of the program is the operating system. One might regard this as the method used to interpret the instructions. It is a significant parameter in that it decides, at least to some degree, the type of hardware that can be used. More importantly, it determines the degree of difficulty with which the system can interact with other software with a different operating system.

It is therefore essential when choosing a particular type of software to select it first on the basis of its performance of the functions that you require, secondly for its operating system which will determine how well it will work with other systems, and will probably also determine the type of hardware on which it will run and thirdly for the ease of modification associated with the language in which it is written.

Increasingly there is a welcome tendency in the Health Service to standardize on a limited number of operating systems such as PICK, VME and UNIX in order to enhance the likelihood of compatibility between different systems linked, for example, to a patient administration system (PAS). However, this initiative is comparatively recent and it will take many years, if ever, to achieve the objective of a unified operating system throughout the Health Service because of the large number of existing and heterogeneous systems.

Operation of a computer system

Putting information into the system: INPUT

Increasingly, users of computer systems are individuals who are not computer operators but are clerical and secretarial, medical or nursing staff who are not interested in how the computer works but rather what it does (Asbury, 1983b). It is therefore necessary for designers of computer systems to make them "user friendly": they must help the user to make the best use of the equipment. This "user friendly" quality manifests itself in features such as the design and layout of the VDU screens requesting or displaying information. When data is being entered at a reception desk, it must be easy for the typist to enter information correctly and as quickly as possible.

When the accuracy of information is vital, the computer may prompt the user to check the information before allowing further information to be put in. Certain data entry may be made mandatory in order to ensure consistency or reliability of information, or for some other purpose. "Help" displays may be available to provide lists, for example, of consultants' names, so that the correct spelling may be obtained, or the correct initials for a particular individual checked before data entry is completed.

Generally this type of information is entered through a keyboard similar to a typewriter, however, other types of data entry are possible: the commonest is the bar code reader (Asbury, 1983b; Arenson, 1984). This may be used in two general forms. Firstly, and more commonly, an X-ray examination number may be provided in bar coded form to select a patient's name and history from the computer store. Similarly, such a system may be used to enter the number and type of X-ray films used during a particular examination by having particular bar codes representing the numbers 1–9, with other codes for different sizes and types of film. Alternatively, bar codes may represent specific textual phrases used to formulate an X-ray report. This obviously facilitates rapid and simple entry of information without using the keyboard. Light pens have been used in the past for this, but more recently the light gun has been introduced with a much faster and more accurate response, as you might notice in your local supermarket!

In the interests of security of data held in the computer it is necessary to have a system of "passwords" which allow individuals access to only certain parts of the program. Alternatively, it is possible to limit the functions of a particular terminal, such as a VDU in a clinical environment, where unauthorized use might be more likely. This ability to restrict the functions of a terminal makes it possible to use it more efficiently by enabling the operator to move more rapidly between, say, two or three selected parts of the program necessary for the function of that terminal.

Setting the system to work: DATA PROCESSING (Asbury, 1983c)

The speed of operation of the system is crucial to its acceptability by the users. Generally, any routine request for information or data entry should produce a response from the computer in less than 1 s, even in the most adverse circumstance, and one would expect a considerably faster response in the majority of circumstances. This may lead to some compromises: for example, patient registration takes precedence over other, less essential areas of activity such as report transcription, or other even less demanding tasks. The response time of the system depends largely on how the programs have been designed, how they operate and the inherent capacity and speed of the computer processor and the associated disc-storage equipment. Poor response time will soon destroy confidence in the system and lead to loss of quality and poorer performance by staff.

Producing the report: OUTPUT (Asbury, 1983b)

The output of the computer will be on either VDUs or printers. Video display units are suitable for enquiry or review of information, but in the radiological context the output of the department is the written report of the radiological examination and therefore printers are an important component in such systems. The type and quality of the printers is an important consideration, and to some extent the choice is dependent on their use. Considerable improvements have been made in matrix printers with the introduction of 24 point matrices, the print quality of which rivals the "letter quality" type of daisywheel printers. Laser printers have the significant advantage of being quiet in their operation, but are expensive. Thermal printers are also quiet, but are relatively slow and their print quality is often less than ideal. In addition, the paper they use is expensive. In general, therefore, the 24 point matrix printers are probably the most suitable at present for all general purposes and are adequate to print bar codes of sufficient quality for good reading reliability. The choice of the speed of printing is important in relation to the volume of data likely to be printed and the acceptable level of noise. Acoustic hoods can be very helpful, although they add to the cost. Most printers will have "tractor feed" for continuous perforated paper, but most printer manufacturers will also provide cut paper feeds for such printers for printing letters and other documents such as patient instructions for radiological examinations.

Types of computer systems

There are three broad groupings into which computers fall (Asbury, 1983a; Greenfield et al, 1984).

Microcomputers. These are better known as personal computers (PCs) of which there is now a very large range.

Minicomputers. These are the most commonly used in commercial and industrial environments and are middle sized in operational terms.

Main-frame computers. These are the large machines used by banks, insurance companies, large scientific organizations and so on.

Microcomputers

There have been remarkable developments in the microcomputer or personal computer area in recent years, with a dramatic improvement in the performance of these machines, associated with falling prices. These machines are generally used as single operating stations with a VDU and printer and up to 60 megabytes (MB) of memory. This was, until recently, more than three times the storage capacity of the DEC PDP 11/34 radiology minicomputer system in the department at Stobhill General Hospital, Glasgow!

However, it is now possible to run microcomputers in a network (Markivee, 1985) in such a way that different functions can be performed by each of the computers, for example, at registration, appointments or the reporting area in a radiology department. This type of system is popular in small businesses where gradual expansion of the system is possible as funds and necessity arise. There are advantages in that failure of any part of the system does not lead to a collapse of the whole system. The parts are interchangeable, and so critical functions can be maintained. However, the system is relatively costly as many work stations do not require the capacity of a microcomputer, which may cost as much as six or seven times that of a VDU. Where there are many terminals in the system, additional data storage in the form of a file server is necessary. This unit can be regarded as a small computer controlling a number of disc drives and performing a central memory function for all the microcomputers, and is again relatively costly. A small number of such systems is now available on the radiology market.

A general limitation of micro-based systems, until recently, has been the difficulty of transferring the software to larger computer systems, as the needs of the user increase. There have been significant developments in this area to overcome this problem.

Minicomputers

Many minicomputers are now effectively indistinguishable in functional terms from modern large capacity microcomputers. The terms are therefore more difficult to define. A minicomputer system is composed of the traditional components of VDUs, a printer, a host computer and storage devices such as hard disc drives or even laser drives. Generally, the system is capable of handling more data simultaneously more rapidly (multitasking) than micro-based systems. The previous difficulty of linking micros to the mini system has been overcome and so it is possible to have facilities in a microcomputer to manipulate information obtained from the main system. This might take the form of producing a colour graphic display of information. In the past the minicomputer tended to be relatively large, accommodated in steel cabinets 6 feet high, but even this distinction is now disappearing, as many fairly substantial mini systems are accommodated in "suitcase" size cabinets below the operator's desk. However, minicomputers are generally more flexible in their operation, and as a rule have substantially faster operation than micro-based systems. One limitation is the need to provide a second computer in order to ensure absolute continuity of service in the event of failure. Fortunately, modern minicomputer systems are extremely reliable and this is not the significant problem that it once was.

Main-frame computers

As the name suggests these are substantial computers capable of hundreds of thousands of simultaneous tasks and extremely high speed of operation. They are still relatively large physically and require a controlled environment, and are found where large amounts of data must be handled. Many health boards use them for financial and payroll applications. In order to maximize the use of their capacity, they are often linked to several sites, sometimes considerable distances apart. These attributes have made them useful to computer companies offering to provide computer facilities to health authorities in relation to the "Facilities Management" concept recently promoted in the Health Service. Such companies may be able to offer a health authority complete computer support on a remote main-frame computer system which has surplus capacity. This has significant aspects in the care and supervision of the transfer and handling of medically sensitive data.

These machines have the capability of running several different operating systems simultaneously, offering considerable power and flexibility in data handling and exchange between the different operating areas. From the clinical end user's point of view, such developments may appear superficially attractive, but the effectiveness of the system from this standpoint depends on the user's accessability to the system. This may be very uneven if there is a heterogeneous mix of users. For example, if the Finance Department of the Health Board is printing the monthly salaries, this may dominate the machine to the temporary exclusion of some less highly prioritized user (such as the radiology department!), with significant lengthening of the response times. Furthermore, the length and type of communication lines from the user to the computer will have an important effect on the response time. This may not be critical in non-clinical situations, *e.g.* running statistical programs, but we are all familiar with the delays of overloaded airport reservation systems!

Networking

The telephone system is a network that has existed for voice communication for over a century. More recently, data and even images have been communicated effectively. Computer networks are similar in concept as a means of sharing information between a number of users (Digital Equipment Corporation, 1982).

Networks can be local, within an office or building, or more extensively, between different sites in an organization. They are evolutionary, in that, soon after installation additional uses become apparent and additional equipment is connected or interfaced to it and the communication of information enhanced. The speed of information transferred between different parts of the system is determined by the type of cable used and the nature and volume of the data. At one end of the spectrum is the need to connect two PCs in adjacent offices, exchanging simple numeric or textual information. This could be achieved easily by ordinary electrical flex. At the other end, there is the need to transmit a radiographic image instantaneously over several miles: because of the high density of the data in the image, even with the fastest fibreoptic cable, it would take perhaps several minutes to complete the transaction. The commonest cable in use today in networking is high-grade TV cable. This may be used to transmit information of only one type at a time (baseband transmission) or many different types of information simultaneously (broadband transmission). Because of the availability of TV cable it is inexpensive, and high quality data transmission can be readily achieved. Points of contact between the cable and items of hardware are called "nodes" which provide the means for converting the information from the hardware into a form acceptable to the network system and *vice versa.* Until recently, the conversion process was often specific to the supplier of the network, and it was ensured that only his hardware could be connected to it. Nowadays, international agreements are being reached for standardization of such protocols, *e.g.* ACR-NEMA standard 300/85 for image data transmission (American College of Radiology and National Electrical Manufacturers' Association, 1985).

One of the most popular network systems is Ethernet (Digital Equipment Corporation, 1982). In this system the cable (½ inch or ⅜ inch TV coaxial cable) can be installed throughout a building, and as the network is developed, items of hardware can be added at will to perform selected functions. Host computers (*e.g.* mini-computers), file servers, terminal servers (allowing several VDUs to be connected simultaneously), printer servers and even PCs can be connected directly to the cable. Several host computers of different hospital departments can be connected and under specified conditions may exchange data. This is the basis of many hospital PAS arrangements. Such local area networks (LAN) may be linked to other similar networks at some distant site, perhaps another hospital or a main-frame computer at health authority level for central data collection or accounting purposes (Faulkner et al, 1987).

Bounded and unbounded media

Transmission of data has so far been described as conducted by cable, either electrical or fibreoptic: these are bounded media as they are not subject to interference. The information is contained within the cable. Radio transmission by microwave link is a further alternative for data transmission over line of sight distances. This is known as an unbounded medium and is, of course, widely used in telephone systems. It has high quality and capacity and is surprisingly modest in cost when selected for specific applications over relatively short earth distances. Such systems have been developed to link computed tomographic (CT) scanners to remote viewing consoles.

Concerning the application of computer systems in management and operation of radiology departments (Arenson et al, 1979; Arenson, 1984, 1986a, b), there are a number of areas which require particular consideration.

Assessing your existing operational system

The existing manual operational system must be reviewed and, if necessary, improved before you install a computer system. This can be done in two stages, system analysis and definition of problem areas.

Undertake a system analysis

It is essential, before embarking on the purchase or design of a computer system, to carry out a detailed survey of the operation of the department with one of the computer staff, known as a systems analyst. It is his responsibility to get to know the details of what your department does and how it does it in order to tailor the computer system to fit in with your requirements. Time spent on this, which may extend over many weeks if a new system is being developed, will be well repaid by a more effective computer program with fewer problems when it begins to operate.

Define problem areas

Difficulties develop after the installation of a computer because its operation is so rapid that bottlenecks in the manual system soon become apparent: for example, failure to acquire the previous film packet may completely negate any other operational improvements, or high throughput of reports may not be achieved if radiologists fail to make sufficient use of coded reporting. Detailed study and revision of existing systems are necessary to remove bottlenecks, improve poor ergonomic arrangements and establish a well defined and organized flow-line system of operation that will complement the computer system. This cannot be over emphasized.

Preparing a specification for the computer system

Fundamental components

Having analysed the department work flow it is now necessary to identify the particular areas of work in your department that computerization would benefit (Arenson et al, 1979; Sutherland et al, 1980; Arenson, 1984). A number of these are now well established: registration, patient index, report preparation and word processing facilities (Arenson, 1986a), film packet tracking, appointments, disease indexing and statistical packages that will enable the calculation of costs (Levy & Hessel, 1985; Arenson et al, 1988), workloads and so on. A further group of applications is less well established, but these functions will have relevance in particular types of department: systems to instruct and control portering activities, radiographic quality control (Jost, 1986), equipment maintenance and management (Arenson, 1986a), personnel management and electronic mail systems (Rowberg et al, 1985) which can be useful in distributing information through a large department or group of hospitals through the computer network. Other applications include maintenance of a file of interesting teaching cases (Arenson, 1986b), reference listings, structured teaching programmes, and in private practice, billing systems and so on.

With the increasing emphasis on resource management in the Health Service the benefits of having a computer system will become increasingly apparent. Stock control of consumable items becomes possible by frequently using the bar code labels, already present, on items such as catheters, contrast media containers and so on. Stock control of films is well developed in most departments already, but this will be simplified by computer documentation of this information. Departments already involved in resource management recognize that without computerization, the calculation of costs on an ongoing basis would be quite impractical. The production of statistical returns of workload using Korner data also becomes practical and can be used on a day-to-day basis to assist operational aspects of the department, instead of being merely a monthly return. Such information can be captured automatically by the computer system by analysing the information about a patient input at the reception desk. This data is more accurate and more readily available than by conventional manual systems and can be used to assess workloads by clinicians, by firms and by departments, giving much better perspectives of the use of the radiology service. This can be done, in most cases, with little operator intervention using modern software techniques.

Although Jost (1986) has referred to the use of computers in radiological quality control, my own experience of this suggests that computers have only a small part to play in documenting the information and displaying it in an interesting manner, for example as bar codes or graphic displays. However, there is no doubt that a number of the film manufacturers have produced computer systems that go much further and allow a detailed analysis, for example, of processor function when such machines are linked directly to the computer system. However, I suspect this information would be more valuable to equipment engineers than to most radiographers or radiologists.

Recently X-ray equipment that can be linked to administrative computers has become available in this country, where exposure factors can be linked directly to a particular patient's examination, and in the light of EEC Ionizing Radiation Regulations (1988), this may eventually become a requirement in order to monitor patient dosage. Such links could be extremely useful, ensuring accuracy and also avoiding additional radiographer activity in logging the exposure.

Having decided on the functions your department requires, it is wise to proceed gradually, introducing a few functional modules at a time, in order to allow staff to become familiar and develop a relationship with the system and recognize its benefits. Many clerical staff still fear the introduction of computer systems and see them as the potential cause of difficulty or even redundancy.

Potential for development of the system

In a system of any size, potential for development must be provided. Inevitably, as time progresses further applications will be recognized by the users and modifications will become necessary, perhaps in the light of alterations in the department's operation system. Most software houses will provide their own software upgrades free of charge as part of their maintenance contract, but development for your own purposes will usually have to be paid for, unless it is seen by the supplier to have universal application.

A detailed specification for a radiology computer system was developed by the Royal College of Radiologists in conjunction with the Centre for Information Technology (Royal College of Radiologists, 1987). It is available from the General Secretary of the Royal College, together with a check list of important features.

Specification of size and operational requirements

It is possible to calculate the size of the computer storage memory and the memory in the processor by identifying the amount of information which has to be stored and manipulated. Such calculations are best left to the suppliers you select, because at least to some extent the physical size of the system is dependent upon the manner in which the software is written. A crucial point, however, is the size of the memory in the processor, as this determines, to a large extent, the number of tasks which may be carried out simultaneously. This will have an important influence upon the response time. It is therefore essential to ensure that sufficient processor memory is provided in the initial installation to allow for potential development. It used to be considered appropriate to store only a moderate amount of information in an immediately accessible form, so-called "real-time storage", for say a 3-month period. However, the dramatic drop in the cost of storage media makes it quite practical to store data even for a large radiology department in this way for the full statutory period. Such media would include optical discs in addition to large capacity hard or Winchester magnetic discs.

The response time

The response time is the time taken for the computer to respond to a simple enquiry *e.g.* to search for a name on the patient index. It is essential that this should not extend to beyond 1 s during heavy activity in the computer, otherwise typists and secretaries will become frustrated by the perceived delay in the operation of the system. In normal circumstances the response time should be substantially less than this. Of course, longer enquiries, such as statistical analysis of a large data base, may take many minutes, and are usually done during the night or periods of low activity to avoid interference with normal usage.

System housekeeping and back-up

These are processes of sorting and reorganizing the information in the computer and copying information in a regular way to avoid loss of data, should the computer fail. Different methods are used to carry out these tasks. It is necessary to establish that the methods suit the operation of your department. Such activity is usually carried out during the night or at least out-of-hours, and may need to be started by a member of staff at some inconvenient hour. It is also important to establish how the department will continue to operate if there is a computer failure, and to have suitable contingency arrangements (Royce, 1988).

Procurement of a computer system

With the development of an apparent commitment to information technology (IT), the NHS has made some provision to assist would-be users. The "NHS Computer User's Handbook" is a valuable source of information about hardware, software, contact individuals and official organizations in the healthcare computing industry and is reasonably up to date. The South-West Regional Health Authority has been given responsibility as the National Computer Procurement Centre and can provide information and guidance across a wide range of IT companies' products and services, and has recently produced a publication entitled "Purchasers Guide to Nationally Approved Suppliers of IT Products and Services". There is also a Prestel system called the NHS Computer Help-line (Tel. 01-247 0671) which provides similar information, if you have a Prestel compatible micro or terminal.

Once a number of suitable systems have been identified it is essential to see them, if at all possible, in a working department environment in order to check response time and the degree of user friendliness. These factors are very difficult to assess in demonstration systems, where there may be only one terminal in operation and a very limited amount of data stored, which is easy for the computer to sort through.

Another important consideration is the compatibility of the operating system with others in the hospital or district environment, and in particular, with any patient administration system. These are matters, however, that your local computer scientific officer will no doubt have in mind.

In the early years of computer development and the application of computers to radiology departments, it was hoped that their introduction would reduce department costs. In fact it was often suggested that the case for the computer might be made on the basis of such improvements in revenue costings. However, experience has shown that this is rarely the case. Improvements in efficiency may well arise, but these are often indirectly generated by the necessity to improve operational system of the department to meet the requirements of the computer rather than the direct effect of the computer itself. However, the improvement in the overall performance of the department, particularly in terms of the rapidity of turnover of information, should lead to improvements in clinical performance, with the prospect of savings, perhaps in bed occupancy, for example. Improved control of the department may also avoid duplication of examinations and fewer repeat examinations because of lost documentation or film envelopes.

The management of information

It has been said by Gaffney (1983), "Whoever controls the creation and flow of information, controls the distribution of power". This was more recently recognized (The Sunday Times, 2 April, 1989) when it was stated that the position of the secretary who controlled the office computer was challenging the manager who was not computer literate for the control of the business. This may soon become the situation in the NHS as managers hold and manipulate clinical data, perhaps to the detriment of patients, because of a preoccupation with cost effectiveness in a simple numerical terms. If clinicians are going to sustain their position on behalf of patients in their care, it will be increasingly important for them also to maintain effective control of their own information management. Doctors appear to be reluctant to move in this direction and yet, in an increasingly competitive world, it seems imperative if we are to have the information available to maintain and develop the services that we give to our patients. Such information should relate to every aspect of the operation of a radiology department, including staff files, salaries, staff management, stores, maintenance, capital depreciation costs and quality assurance, not only involving radiography but every aspect of department operation including medical audit. The ability to conduct effective medical audit in a radiology department, however, will be prevented until much more extensive hospital information systems are available, which allow comparisons of radiological, clinical and pathological diagnosis and allow the assessment of the interaction between imaging diagnosis and patient management.

This paper has been concerned entirely with the management of textual information. However, picture archiving systems are already available, although at an early stage of development, and it is obvious that the correlation of textual and picture information is central to our work, and inevitably linkages between these systems will need to be developed. Much work needs to be done in this area, as even the most modern CT and magnetic resonance imaging scanner systems use archiving arrangements which rarely enable linkage of examinations carried out on the same patient from time to time, and as yet provide no opportunity to store examination reports. It may be many years before such systems are regarded as a reasonably cost effective alternative to more conventional approaches.

Summary

Although the computer is now becoming more common in radiology departments, where its application is generally in the field of assisting in the operational effectiveness of the department at a clerical and secretarial level, the implementation of the White Paper "Working for Patients" will make it increasingly important for the radiologist in charge of a department and the superintendent radiographer to have the facts and figures of the operation of the department at their fingertips. This will be to the benefit of our patients, as it can only lead to an improvement in the effectiveness of our activities. Such information will also give us greater confidence in discussion with clinical colleagues, by providing specific facts relating to unrealistic use of the services we provide.

Glossary of terms

The computer is dominated by specialists who revel in using jargon. Much of this is unnecessary, and it makes understanding difficult for those on the outside. This glossary is by no means comprehensive, but explains some of the more commonly used terms.

Address. Information in a computer is moved around from place to place; these "places" are called "locations" or "addresses".

Applications software. A computer program designed for a particular purpose for the user. This should be contrasted with the system software which is responsible for running the computer *e.g.* the operating system.

ASCII. American Standard Code for Information Interchange. This is the internationally accepted code that represents numbers, letters and symbols with unique binary bode values which the computer can understand.

Bar code. Pattern of printed lines containing information, usually about an object. However, it can be used to enter any kind of information into a computer very rapidly by scanning it with a light pen or light gun.

Basic. The most popular language for microcomputers: Beginners All-purpose Symbolic Instruction Code.

Binary. A way of counting using only two alternative values: 0 or 1. This is the language that computers work in. All higher level languages are eventually converted to binary.

Bit. A binary digit: "0" or "1".

Byte. "By eight". Usually a byte means a group of eight bits. One byte contains enough information to represent one ascii character.

Character. A general-purpose expression for numerals, letters and symbols that a computer can display or print.

Disc. Flat magnetic disc which is rotated very rapidly in a disc drive on which data may be stored or retrieved very rapidly. Discs are either flexible (floppy) or hard (rigid). Hard discs are sometimes known as Winchester discs and have substantially higher capacity than the floppy discs. Recently, optical disc drives have become available and have significantly greater storage rates, where information is stored and read by laser (laser discs).

Expert system. Complex programs with large data bases of information capable of logical decision making. Some are already in use in clinical evaluation.

High level language. Programming language where the program uses instructions which are close to the ordinary familiar language of the programmer, rather than machine code.

Interface. The boundary between two parts of a computer system, usually an electronic circuit.

Memory. A computer's memory is a device or series of devices capable of storing information temporarily or permanently in the form of patterns of binary information. It may be internal within the computer where it is usually composed of silicone chips, or externally in the form of magnetic or optical discs or magnetic tape. Memory may be "volatile" when it is lost when power is switched off or "non-volatile" when it is not erased in these circumstances.

Microprocessor. Used as a synonym for a microcomputer but correctly is the central chip containing the control unit for the computer.

Network. A system where a number of computers or terminals with other components like disc drives and printers are linked together.

Operating system. A program permanently in a computer which supervises the running of applications programs and controls the operations of various input and output devices, such as a video display unit, printer, light pen etc.

Peripherals. Items of a computer system which connect in different ways to the central processor and form its input and output devices *e.g.* printers, VDUs, disc drives etc., otherwise known as "terminals".

Programmer. An individual who is responsible for writing software programs.

System analyst. A member of computer staff responsible for analysing and documenting the operational aspects of the organization to be supported by a computer system in order to allow the program to be created.

Word. When a computer operates it deals with groups of bits at a time. the minimum number of bits which the central processor handles at any one time is called a "word". In a microcomputer the "word" used to be eight bits long, but more recently 16- and even 32-bit processors have been introduced, which increases the speed of operations significantly.

References

AMERICAN COLLEGE OF RADIOLOGISTS AND NATIONAL ELECTRICAL MANUFACTURERS' ASSOCIATION, 1985. *No. 300+1985 for Digital Imaging and Communications Committee* (ACR—NEMA, USA).

ARENSON, R. L., 1984. Automation of the radiology management function. *Radiology, 153*, 65–68.

——1986a. Office automation. *Radiologic Clinics of North America, 24*, 87–96.

——1986b. Teaching with computers. *Radiologic Clinics of North America, 24*, 97–104.

ARENSON, R. L. & LOUDON, J. W., 1979. Comprehensive analysis of radiology operations management computer system. *Radiology, 133*, 355–362.

ARENSON, R. L., VANDER WOORDE, F. & STEVENS, J. F., 1988. Improved financial management of the radiology department with a microcosting system. *Radiology, 166*, 255–259.

ASBURY, A. J., 1983a. ABC of computing: what is a digital computer? *British Medical Journal, 286*, 1717–1719.

——1983b. ABC of computing: input, output and the user. *British Medical Journal, 286*, 1799–1801.

——1983c. ABC of computing: the processing unit and the programme. *British Medical Journal, 286*, 1878–1879.

——1983d. ABC of computing: auxiliary storage. *British Medical Journal, 286*, 1952–1953.

BRADBURN, R., DE BONO, P. & LAURIE, P., 1982. *The Computer Book* (BBC, London).

FAULKNER, J. J., MOSEBY, J., WILSON, S. J. & SMITH, N. A., 1987. Transformation achieved by integration. *British Journal of Healthcare Computing, 4*, 19–22.

GAFFNEY, C. T., 1983. *The impact of office automation on power in organizations* (presentation at AFIPS Office Automation Conference).

GREENFIELD, G. & HUBBARD, L. B., 1984. *Computers in Radiology* (Churchill Livingstone, London).

DIGITAL EQUIPMENT CORPORATION, 1982. *Introduction to Local Area Networks* (DEC, Alabama).

JOST, R. G., 1986. Monitoring department efficiency and quality. *Radiologic Clinics of North America, 24*, 97–104.

LEVY, J. M. & HESSEL, S. J., 1985. Practical value of computer literacy: 3: non-imaging computer applications in radiology. *American Journal of Roentgenology, 145*, 1089–1090.

MARKIVEE, C. R., 1985. Networking of microcomputers in the radiology department. *American Journal of Roentgenology, 145*, 849–853.

NHS, 1988. *NHS Computer User's Handbook*. Ed. by Hazel Coad (The British Journal of Healthcare Computing, London).

——1988. *NHS Purchaser's Guide to Nationally Approved Suppliers of Information Technology Products and Services* (NHS Computer Procurement Centre, Bristol).

ROWBERG, A. H., NEWELL, J. D. & HUNTER, T. B., 1985. Telecomputing in radiology. *American Journal of Roentgenology, 145*, 411–413.

ROYAL COLLEGE OF RADIOLOGISTS, 1987. Functional specification for a radiology computer system. (RCR and NHS Centre for Information Technology, London).

ROYCE, R., 1988. Keep the user satisfied. *British Journal of Healthcare Computing, 5*, 47.

SUTHERLAND, G. R. & SHIMMINS, J., 1980. Application of an administrative computer to departments of diagnostic radiology. *Health Bulletin, 13*, 203–207.

SUTHERLAND, G. R., 1983. Why are we not using computers in our department? *Clinical Radiology, 34*, 215–221.

1990, *The British Journal of Radiology*, *63*, 97–100

Vasopressin release in response to intravenously injected contrast media

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Abstract. We have previously reported that intravenously administered contrast media produce a rise in plasma vasopressin (antidiuretic hormone) concentrations. We have now shown that this occurs both when contrast medium is injected into a peripheral vein and when it is centrally injected into the right atrium. The peak vasopressin concentration recorded varies with the osmolality of the contrast medium. The vasopressin response was greater when contrast agent was centrally injected.

The injection of a bolus of contrast medium into the circulation has a range of effects and initiates homeostatic response in the cardiovascular system.

The main effects are volume expansion, vasodilatation and a fall in systemic blood pressure, together with a short term reduction in cardiac output. The main homeostatic response is autonomic activity mediated by baroreceptors sensing a fall in systemic blood pressure.

In our previous paper (Trewhella et al, 1987) we showed a prompt rise in plasma vasopressin (AVP) concentrations following the peripheral injection of higher osmolality contrast media and we suggested that this response was related to the injected osmolar load.

Vasopressin is a potent vasoconstrictor in the renal vascular bed and can cause shifts of intrarenal bloodflow distribution (Walker et al, 1978). The finding of elevated plasma AVP concentrations after contrast administration may therefore be relevant to reports of reduced renal blood flow after contrast medium administration and possibly to contrast media related nephrotoxicity.

To assess further the relationship between osmolar load and AVP concentration we have measured the AVP response to a peripherally injected contrast agent of much lower osmolality, iopamidol 300 mgI/ml (Niopam 300, Merck/Bracco).

Centrally injected contrast agents might be expected to cause an even larger rise in AVP concentrations than those delivered into a peripheral vein, since both the peak osmolality and the rate of rise of osmolality will be higher.

However, direct right atrial injection at digital subtraction angiography (DSA) should also give good stimulation of right atrial stretch-receptors. Animal studies show that sudden right atrial distension causes a fall in AVP levels (Abed et al, 1982), whilst volume expansion in man has also been shown to lower AVP levels (Forsling et al, 1986).

So, centrally injected contrast media could potentially produce either a rise in plasma AVP in response to the injected osmolar load or an AVP fall resulting from the volume load sensed by atrial stretch-receptors.

Therefore we measured the AVP response to the central venous injection of two contrast media during DSA. The agents used were iopramide 370 mgI/ml (Ultravist, Schering Health Care), an agent of lower osmolality and sodium meglumine diatrizoate 370 mgI/ml (Urografin, Schering Health Care), of higher osmolality. The osmolalities of the contrast media referred to are listed in Table I.

Patients and methods

Peripheral injections

Eight patients were selected from a routine intravenous urogram (IVU) list. Patients taking drugs known to influence AVP levels and those with renal, cardiac or alcohol related disease were excluded as in our previous study. Blood was taken for the assay of plasma AVP 1 min before the injection of contrast medium and at 1, 10 and 20 min after injection of 50 ml iopamidol 300 mgI/ml into a peripheral arm vein as a bolus.

Central injections

Eleven patients were selected from an intravenous DSA list. A 5 F catheter was passed into the right atrium, and 40 ml of either sodium meglumine diatrizoate 370 mgI/ml or iopramide 370 mgI/ml was injected at 20 ml/s and blood samples taken via a separate

Table I. Osmolalities of contrast media

Contrast medium	mOsmol/l
Iopamidol 300 mgI/ml (Niopam 300)	616
Sodium iothalamate 420 mgI/ml (Conray 420)	2496
Sodium meglumine diatrizoate 325 mgI/ml (Urografin 325)	1650
Sodium meglumine diatrizoate 370 mgI/ml (Urografin 370)	2150
Iopramide 370 mgI/ml (Ultravist 370)	774

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indwelling venous cannula. Blood samples were taken for assay of plasma AVP before contrast and at 1, 5 and 10 min after contrast medium administration. The sampling times were chosen because we felt it likely that an earlier response would result from central injections at 20 ml/s than from peripheral injections.

In both peripheral and central studies, patients were instructed to have nothing to eat or drink for at least 4 h prior to the study, but no attempt at dehydration was made. Our previous study showed that the degree of fluid intake restriction commonly practised prior to an IVU does not significantly elevate AVP concentrations.

Blood samples were immediately chilled on ice, then centrifuged at 4°C and the plasma separated and frozen awaiting assay. Determination of plasma vasopressin was by radioimmunoassay as described by Aziz et al (1981). The inter- and intra-assay variation coefficients for AVP were 11.9% and 7.7% respectively.

Assay gave absolute values for plasma AVP concentration. Incremental AVP concentrations were also calculated. Statistical analysis was performed by analysis of variance (Kruskal–Wallis) by taking areas under the response curve of log-transformed data using both the absolute and incremental data.

Results

Peripheral injection data

Intravenously injected iopamidol produced an immediate rise in plasma AVP, and the concentrations then declined as shown in Fig. 1. Data showing the AVP responses to two agents of higher osmolality: sodium meglumine diatrizoate 325 mgI/ml and sodium iothalamate 420 mgI/ml, from our previous study are included for comparison.

There is a significant difference between the responses to iopamidol and sodium iothalamate ($p < 0.01$) but not between iopamidol and sodium meglumine diatrizoate.

Central injection data

Injections of iopramide 370 mgI/ml and sodium meglumine diatrizoate 370 mgI/ml both resulted in elevated plasma AVP concentrations as shown in Fig. 2. The response to sodium meglumine diatrizoate was significantly greater ($p < 0.01$).

Comparison of peripheral and central data

The data are not statistically comparable because of the number of variables involved. However, the results suggest that there is a greater response to central injections of 40 ml sodium meglumine diatrizoate 370 mgI/ml (2150 mOsmol/l) than to peripheral injections of 50 ml sodium meglumine diatrizoate 325 mgI/ml (1650 mOsmol/l). The vasopressin concentrations after centrally injecting 40 ml sodium meglumine diatrizoate 370 mgI/ml were as high as those seen after peripherally injecting 60 ml sodium iothalamate (2496 mOsmol/l) even though the latter represents a substantially greater osmotic load.

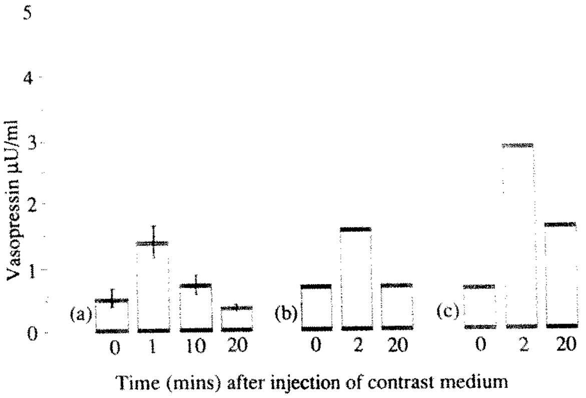

Figure 1. Mean vasopressin responses to peripheral contrast media. (a) Iopamidol 300 mgI/ml (n = 7), (b) sodium meglumine diatrizoate 325 mgI/ml and (c) sodium iothalamate 420 mgI/ml.

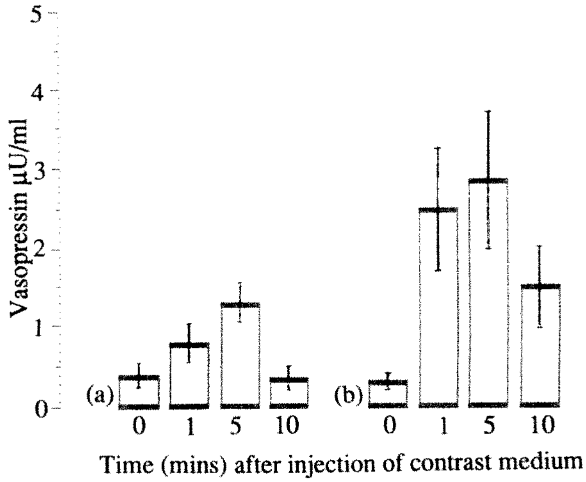

Figure 2. Mean vasopressin responses to central injections of contrast media. (a) Iopramide 370 mgI/ml (n = 4) and (b) sodium meglumine diatrizoate 370 mgI/mg (n = 7).

Discussion

The results confirm our previous observation (Trewhella et al, 1987) that plasma AVP concentrations rise after the intravenous administration of a range of contrast media.

The rapid response and subsequent early fall of AVP concentrations suggest that it is the transient rise in osmolality rather than any prolonged change which is the stimulus to vasopressin release. Our earlier work showed no significant change in plasma osmolality at 2 and 20 min after the injection of 60 ml sodium iothalamate 420 mgI/ml.

There is also a relationship between the osmolality of the injected contrast agent and the magnitude of the response, with higher AVP concentrations being seen with the media of higher osmolality both with central and peripheral injections. The relationship may not be linear, and this may explain the similar responses to peripherally injected iopamidol and sodium meglumine diatrizoate.

The apparently increased response to centrally injected media may be explained by considering the role of vasopressin in osmoregulation. Robertson et al (1976) have shown in man that the size of the AVP response to rising osmolality is proportional to both the magnitude of the rise in osmolality and the rate of its rise. On the basis of their observations, one would predict that a hyperosmolar bolus would lower the threshold and increase the sensitivity of the AVP response to rising osmolality. With the extremely rapid delivery of a hyperosmolar bolus during DSA, the peak osmolality achieved and the rate of rise of osmolality should be greater than those with peripherally injected contrast media, so that a greater AVP response would be expected.

Studies in animals (Abed et al, 1982) and in man (Forsling et al, 1986) have shown that right atrial distension and volume expansion respectively can inhibit AVP release. Furthermore, Robertson et al (1976) have shown that alterations of plasma volume influence the osmotic release of vasopressin, an increase in volume reducing the response. Such a mechanism may have been operating here, as the concentration of AVP 1 min after centrally injecting iopamidol 370 was less that seen 1 min after peripherally injecting iopamidol 300, despite the fact that the former has a higher osmolality and was delivered much more rapidly.

Renovascular responses to contrast media

Our results may help to explain the renovascular responses to contrast media that have been reported.

Talner et al (1968) showed a reduction in renal blood flow of 10–20% 1 min after the injection of contrast media into the renal artery of anaesthetized dogs. They also found a similar fall in renal blood flow after injecting 4.5% NaCl, but no significant fall with isotonic 0.9% NaCl. This suggested that the osmolality of the injected solution was the most likely determinant of the fall in renal blood flow.

A biphasic change in blood flow in the renal artery during renal arteriography has been reported by Russell and Sherwood (1974). They found a rise in blood flow 10 s after the injection of contrast medium, followed by a fall 35–45 s after the contrast injection. The rise in blood flow depended on the cation used in the contrast medium, whereas the later reduction in blood flow was greater with the media of higher osmolality. The dimers studied, sodium and meglumine iocarmate (1102 mOsmol/l) resulted in a 10% fall in renal blood flow whilst the monomers, sodium and meglumine iothalamate (1485 mOsmol/l) showed a 30% fall in renal blood flow.

The role of vasoconstrictor hormones in this response was investigated by Katzberg et al (1982) in anaesthetized dogs. They considered angiotensin II and the prostaglandin, thromboxane as possible humoral mediators of the response. Studying the vasoconstrictor response of the renal artery to a bolus of 4 ml sodium meglumine diatrizoate 76%, they confirmed the biphasic response of renal arterial blood flow, with the maximum decrease in renal blood flow being seen at between 50 and 70 s after the administration of contrast agent. In separate studies, they inhibited the action of angiotensin II at the smooth muscle receptor level with saralasin, an antagonist of angiotensin II, and inhibited prostaglandin formation with indomethacin. In both cases, the response to contrast medium was unchanged, leading them to conclude that neither hormone mediated the response.

There is considerable evidence that vasopressin is a potent vasoconstrictor at physiological plasma concentrations both in animals and man (Cowley et al, 1983). Vasopressin has also been shown to have a vasoconstrictor action specifically in the renal artery in experimental animals. Bennett et al (1987) studied regional vascular responses to vasopressin in conscious Long Evans rats, and found that about 1 min after administration of AVP, there was renal arterial vasoconstriction with an increase in renal arterial resistance of 41%.

We have measured elevated AVP concentrations within 1 min of peripheral venous injection of contrast media so that the time courses of the contrast induced AVP response and of contrast media induced renal artery vasoconstriction are comparable. The timing of the vasoconstrictor response to the administration of AVP in rats is also similar.

It is also interesting that the reduction in renal artery blood flow is proportional to the osmolality of the injected contrast bolus (Russell & Sherwood, 1974). We have shown the magnitude of the vasopressin response also to be related to the osmolality of the injected contrast agent.

Whilst these considerations do not prove that the contrast media induced renal vasoconstriction is mediated by vasopressin, the data is compatible with such a role for AVP.

Contrast agent associated nephrotoxicity

The possible role of vasoconstrictor hormones in this phenomenon has been considered by others (Katzberg et al, 1982). Certainly, vasopressin is a potent vasoconstrictor and some of the risk factors for contrast media associated nephrotoxicity are themselves associated with elevated AVP concentrations. Significant dehydration and a large dose of contrast medium will result in a rise in plasma AVP, whilst AVP concentrations rise with increasing age, a trend which is particularly marked in patients with heart-failure (Rondeau et al, 1982).

However, the role of the vasopressin response to contrast media in contrast media induced nephrotoxicity remains speculative, because the rise in plasma AVP we have seen is relatively modest and transient.

References

Abed, J. S. M., Forsling, M. L. & Nashat, F. S., 1982. On the nature of the diuresis produced by rapid infusion of blood into the left atrium of anaesthetised, thoracotomised greyhounds. *Journal of Physiology, 330,* 31.

AZIZ, L. A., FORSLING, M. L. & WOOLF, C. J., 1981. The effect of intracerebroventricular injections of morphine on vasopressin release in the rat. *Journal of Physiology, 311,* 401–410.

BENNETT, T., COMPTON, A. M. & GARDINER, S. M., 1987. Differential regional vascular responses to vasopressin (AVP) and neuropeptide Y (NPY) in conscious Long Evans rats. *Journal of Physiology, 377,* 188.

COWLEY, A. W., QUILLEN, E. W. & SKELTON, M. M., 1983. Role of vasopressin in cardiovascular regulation. *Federation Proceedings, 42,* 3170–3176.

FORSLING, M. L., MACGREGOR, G. A. & SAGNELLA, G. A., 1986. A comparison of the vasopressin response to saline infusion and to changes in dietary sodium in the human. *Journal of Physiology, 377,* 69.

KATZBERG, R., MEGGS, L., SCHULMAN, G. & HOLLENBERG, N., 1982. Contrast medium-induced renal vasoconstriction and endogenous vasoconstrictor hormones. *British Journal of Radiology, 55,* 266–268.

ROBERTSON, G. L., SHELTON, R. L. & ATHAR, S. 1976. The osmoregulation of vasopressin. *Kidney International, 10,* 25–37.

RONDEAU, E., DE LIMA, J. & CAILLENS, H., 1982. High plasma antidiuretic hormone in patients with cardiac failure: influence of age. *Minutes of Electrolyte Metabolism, 8,* 267.

RUSSELL, S. B. & SHERWOOD, T., 1974. Monomer/dimer contrast media in the renal circulation: experimental angiography. *British Journal of Radiology, 47,* 268–271.

TALNER, L. B. & DAVIDSON, A. J., 1968. Renal haemodynamic effects of contrast media. *Investigative Radiology, 3,* 310–317.

TREWHELLA, M., FORSLING, M. L., RICKARDS, D. & DAWSON, P., 1987. Dehydration, antidiuretic hormone and the intravenous urogram. *British Journal of Radiology, 60,* 445–447.

WALKER, L. A., GERBER, J. G., FROHLICH, J. C. & NIES, A. S. 1978. Redistribution of intrarenal blood flow following ADH administration: lack of inhibition by blockade of cyclooxygenase. *Prostaglandins in Medicine, 1,* 295–303.

1990, *The British Journal of Radiology*, *63*, 101–107

Magnetic resonance imaging of the normal prostate at 1.5 T

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Abstract. Prostatic magnetic resonance images of 22 male volunteers less than 30 years old and with no known genito-urinary tract disease were obtained at 1.5 T. Normal anatomical features of the prostate were studied with spin–echo techniques. Different zones of the normal gland are shown by T_2-weighted images: the anterior fibromuscular fascia, the central prostate, the peripheral prostate and the periurethral zone can be differentiated. The normal prostate gland is shown on T_1-weighted images as a homogeneous appearance. It is important to recognize the normal zonal anatomy of the prostate since prostatic disorders arise in different anatomical zones.

Previous papers have reported results of magnetic resonance imaging (MRI) of the prostate with lower field strengths (Hricak et al, 1983; Bryan et al, 1983; Berry et al, 1984; Poon et al, 1985; Gevenois et al, 1987a) and higher field strengths (Sommer et al, 1986; Philips et al, 1987a, b). The purpose of the following prospective study is to describe the anatomical aspects of the normal prostate and its adnexa. These features were studied with T_2-weighted images, since T_1-weighted images do not show any differentiation in the prostate gland.

Materials and methods

We prospectively studied 22 healthy volunteers, with no known genito-urinary tract disorders, ranging in age from 21 to 30 years. Magnetic resonance images were obtained with a 1.5 T superconducting magnet (Philips S15 Gyroscan), with a display matrix size of 256 horizontal by 256 vertical elements. A body coil with a field of view of 400 mm was used. Four data acquisitions were averaged for each image. Transaxial and sagittal images were obtained from each subject and, in addition, coronal images were obtained in two volunteers. All images were created using a two-dimensional Fourier transform technique.

The same protocol for data acquisition was used. The examinations began with a T_1-weighted sagittal multislice scan (spin–echo (SE), time to repeat (TR) 350, time to echo (TE) 20, two excitations) for positioning the prostate (Fig. 1). A T_2-weighted transaxial multislice scan (SE, TR 2000, TE 50–100, two excitations) was then obtained with sections of 5 mm with 0.5 mm gaps. In two cases, additional coronal T_2-weighted scans were obtained. A 1 h time limit was set for the examination of each volunteer.

The appearances of the prostate, urethra, periprostatic fascia and venous plexus were analysed to determine anatomical detail and signal features.

Results

The prostate showed a homogeneous low signal on T_1-weighted images in all 22 volunteers (Fig. 1). Long TR/TE images (T_2-weighted) demonstrated four

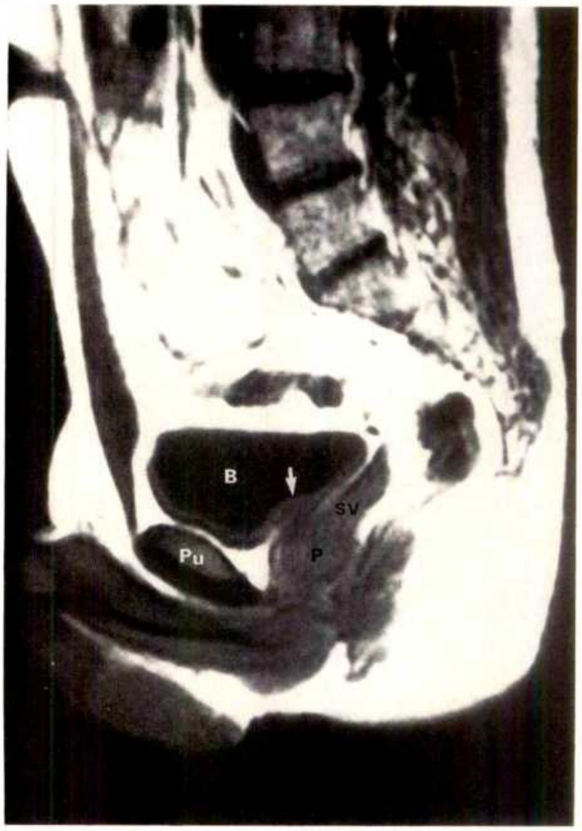

Figure 1. On a sagittal SE 350/20 image of a young adult, the prostate (P) shows an intermediate homogeneous signal. The bulging of the bladder wall is always present (arrow). The seminal vesicles (SV) appear as a low signal (B = bladder, Pu = pubis).

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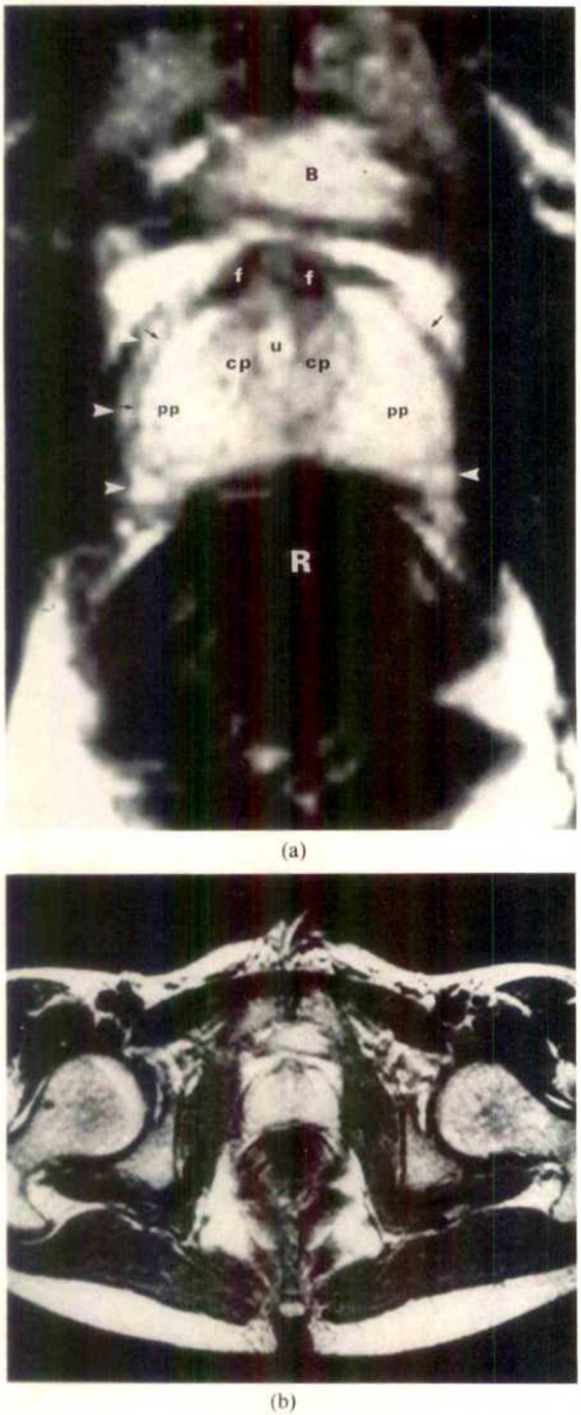
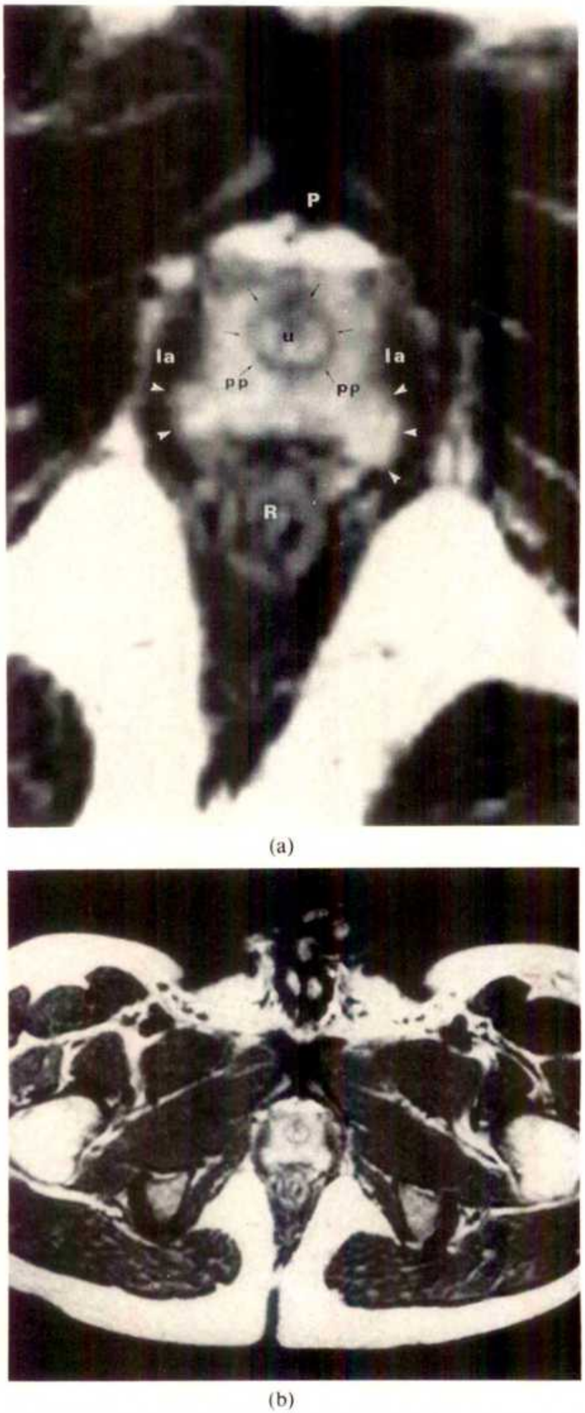


(a)

(b)

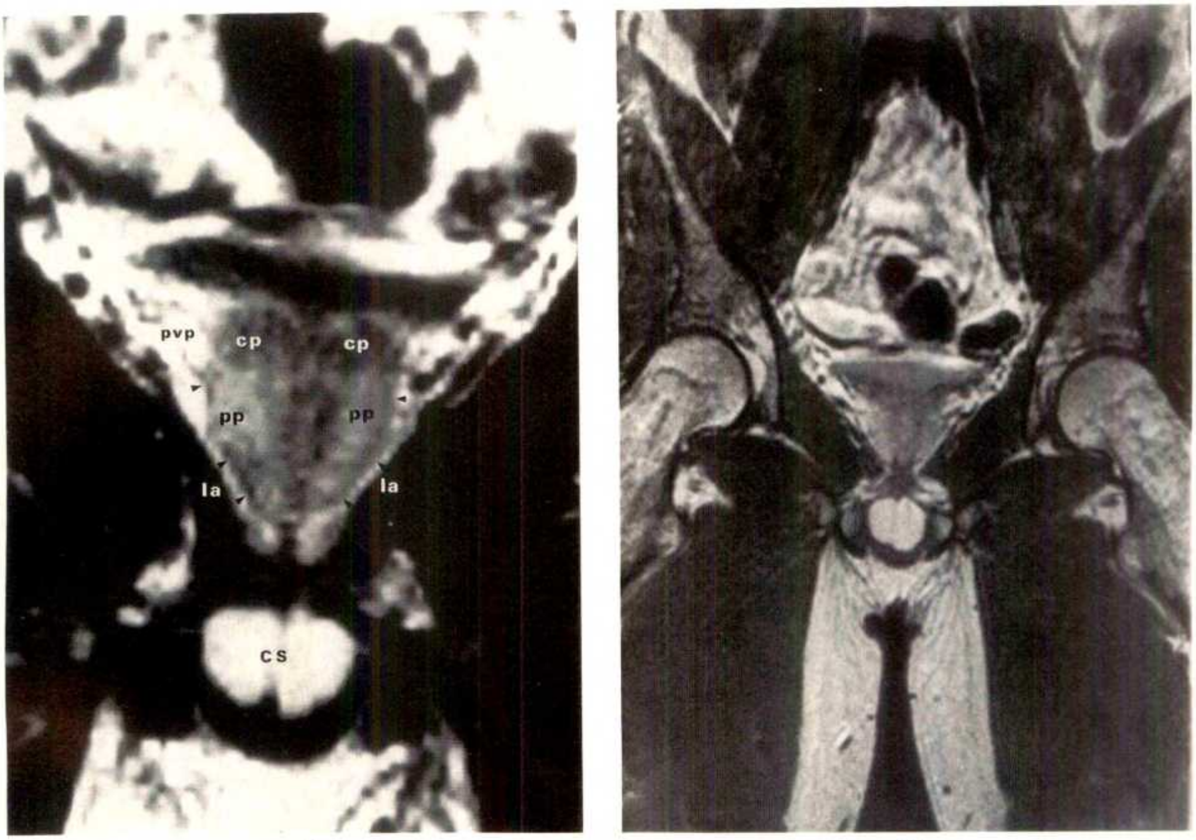
Figure 2. On an axial SE 2000/50 image from the upper half of the prostate, the prostatic zonal differentiation is demonstrated, with the peripheral prostate (pp) being of higher signal intensity than the central prostate (cp). Anterior to the urethra (u) is a zone composed of fibromuscular stroma (f). The prostatic venous plexus (arrow heads) is seen posterolaterally, and the prostatic capsule is visualized (dark arrows) (B = bladder, R = rectum).



(a)

(b)

Figure 3. On an axial SE 2000/50 image from the lower half of the gland, peripheral prostate (pp) is discernible. The urethra (u) is surrounded by a thin low-signal margin (dark arrows). The prostatic venous plexus is seen posterolaterally (arrow heads) (P = pubis, la = levator ani muscle, R = rectum).



(a) (b)

Figure 4. A coronal SE 2000/50 image shows the low-signal intensity of the central prostate (cp), which is lower than the peripheral prostate (pp). The prostatic capsule is discernible (arrow heads). The prostatic venous plexus (PVP) is visualized superolaterally. (la = levator ani muscle, cs = corpus spongiosum.)

separate zones within the gland in all cases. This zonal distinction was well defined on axial images but was also discernible on coronal images (Figs 2, 3).

McNeal describes four different anatomical regions of substantially different composition (McNeal, 1978, 1980a). One large region, the anterior fibromuscular stroma which is up to one third of the mass of the organ, is entirely non-glandular, consisting mainly of smooth muscle fibres. Another region surrounds the proximal or preprostatic half of the prostatic urethra above the verumontanum. This is a complex transitional region of mixed glandular and non-glandular tissue, which in the normal prostate is very small. The peripheral zone is the largest of the two major glandular regions of the prostate and represents roughly 75% of the total glandular tissue. The central zone is the second component of the functioning glandular prostate and makes up about 25% of its mass. It completes the proximal quadrant of the glandular tissue above and behind the verumontanum (McNeal, 1980a). The four zones visible by MRI were as follows (Fig. 2).

a) A very low-intensity anterior region with maximal thickness in the images through the upper portion of the prostate.

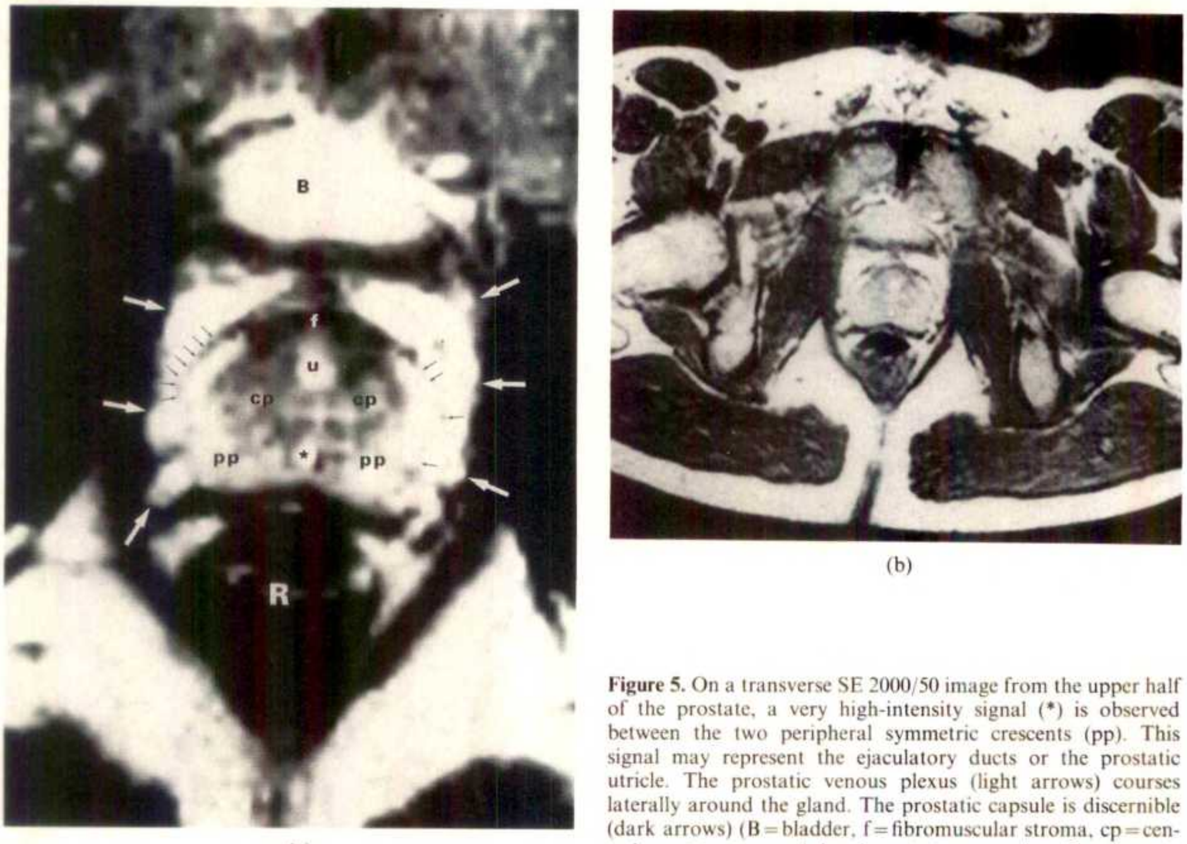
b) Two peripheral posterior symmetric crescents of high signal intensity.

c) An intermediate-intensity region between these two regions in the central portion of the gland. This region is identifiable only on scanning the upper half of the prostate.

d) A small circular area with a high signal lying posterior to the dark anterior region and in the anterior third of the gland. This region is bordered by a thin low-signal margin in the lower half of the gland (Fig. 3). This small circle is thought to correspond to the urethra, surrounded by periurethral glands. The verumontanum was never seen.

These four regions were observed in all cases. The T_2-weighted coronal image through the midportion of the prostate showed a zone of high intensity inferior and lateral to a region of lower intensity (Fig. 4).

Between the two peripheral symmetric crescents, a high signal intensity was observed in three cases (Fig. 5). In one case, three points of quite high intensity were



(a)

(b)

Figure 5. On a transverse SE 2000/50 image from the upper half of the prostate, a very high-intensity signal (*) is observed between the two peripheral symmetric crescents (pp). This signal may represent the ejaculatory ducts or the prostatic utricle. The prostatic venous plexus (light arrows) courses laterally around the gland. The prostatic capsule is discernible (dark arrows) (B = bladder, f = fibromuscular stroma, cp = central prostate, pp = peripheral prostate, u = urethra, R = rectum).

seen, corresponding to the region of the ejaculatory ducts and prostatic utricle. In 10 cases, a thin rim of low signal intensity was poorly seen at the periphery of the gland on T_2-weighted scans, which may correspond to the prostatic capsule proper (Figs 2, 4–6).

The relationships between the prostate gland, the bladder floor, the rectum, the venous plexus within the periprostatic fat, the symphysis pubis and the muscles were well seen. On the midline sagittal scan, a normal bulging of the infero-posterior bladder wall was always present (Fig. 1). On T_2-weighted images, a periprostatic zone with high signal intensity was observed, representing the periprostatic venous plexus (PVP) in fatty tissue (Figs 2–5), seen in the posterolateral and lateral periprostatic tissue, but never in the posterior space between the prostate and rectum. In the coronal scan, the relationship of the prostatic gland to the urogenital diaphragm was well defined (Fig. 6).

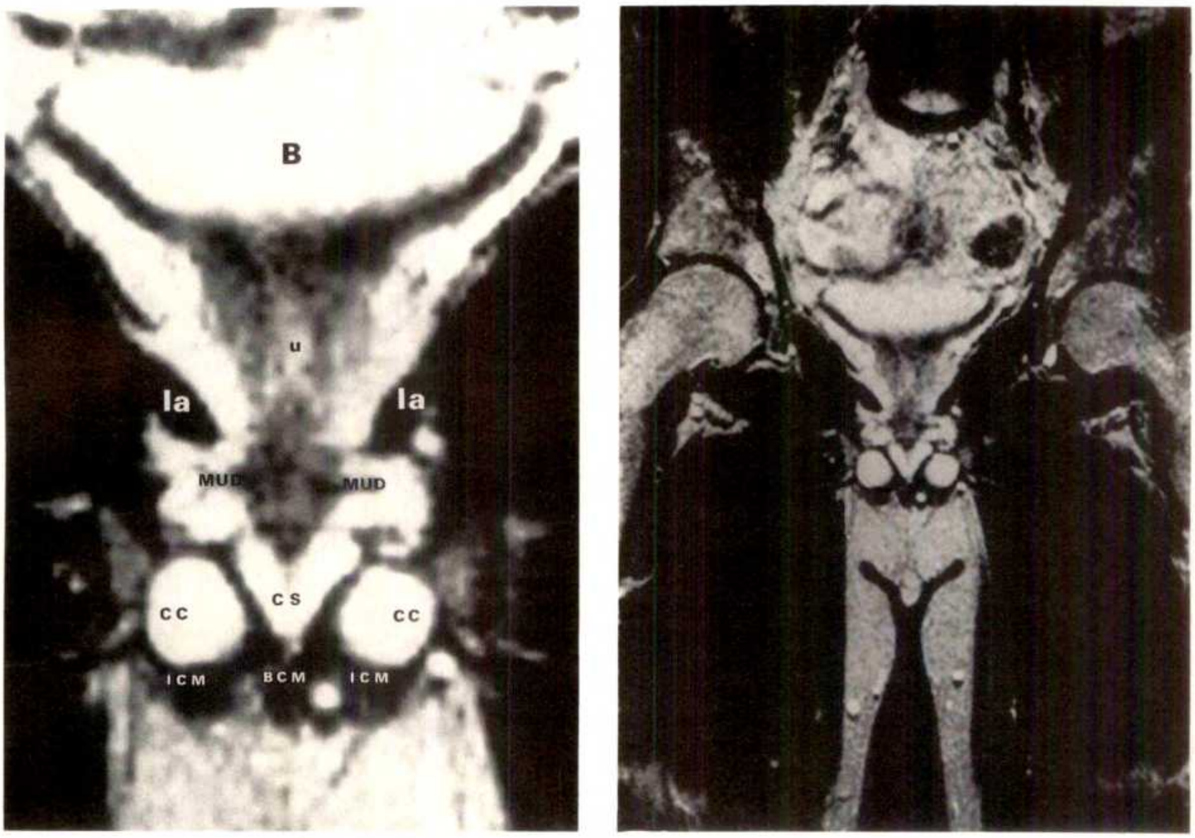
The seminal vesicles were well identified in all cases. The normal signal was always symmetrical, and changed from low intensity on T_1-weighted images (Fig. 1) to high intensity on T_2-weighted images (Fig. 7). The ampulla of the ductus deferens could not be differentiated from the seminal vesicles.

Discussion

Magnetic resonance imaging provides an ideal anatomical image of the prostate. Spin–echo T_2-weighted images obtained at 1.5 T allow distinction between peripheral and central zones and may reveal very small structures such as the urethra or ejaculatory ducts.

Historically, the study of the anatomy of the prostate has been characterized by a proliferation of contradictory findings (McNeal, 1980b). McNeal (1980a) has defined a peripheral and a central zone, the histological differentiation of which leads to a zonal distribution of diseases. Cancer and benign prostatic hyperplasia (BPH) arise mainly in the peripheral and central zones, respectively (Edwards et al, 1953; Franks, 1954; McNeal, 1969; McNeal, 1978). Magnetic resonance depiction of the zonal anatomy of the prostate corresponds to McNeal's description (McNeal, 1972, 1980a). McNeal described an anterior fibromuscular stroma, which corresponds to the dark anterior signal (Figs 2, 5). Leiomyomas arising from this stroma have been described (Gevenois et al, 1987b).

The central zone appears on T_2-weighted images as an intermediate-intensity signal and the peripheral zone as a high-intensity signal (Fig. 2). The biochemical reasons



(a)

(b)

Figure 6. A coronal SE 2000/50 image shows the prostatic urethra (u) and the relationships between the prostate and the perineum. (B = bladder, la = levator ani muscle, cc = corpora cavernosa, cs = corpora spongiosum, ICM = ischiocavernous muscle, BCM = bulbocavernous muscle, MUD = muscles of the urogenital diaphragm).

for this difference are not known. The peripheral zone should contain more free water than the central zone, and the central zone more than the fibromuscular stroma. The definition of these zones depends on differences in gland architecture. The peripheral zone ducts are long, narrow and straight, with short terminal branches ending in small, simple, round acini. The central zone ducts are larger with more complex arborization. They produce large acini of irregular contour, partially compartmentalized by septa. The peripheral zone epithelium consists of pale cells in a simple columnar arrangement with basal, small dark nuclei. The central zone cells have granular, opaque cytoplasm (McNeal, 1980a). This striking histologic difference suggests a great difference in biological functions. The differences in signals by MRI confirm a chemical difference between central and peripheral glandular tissue.

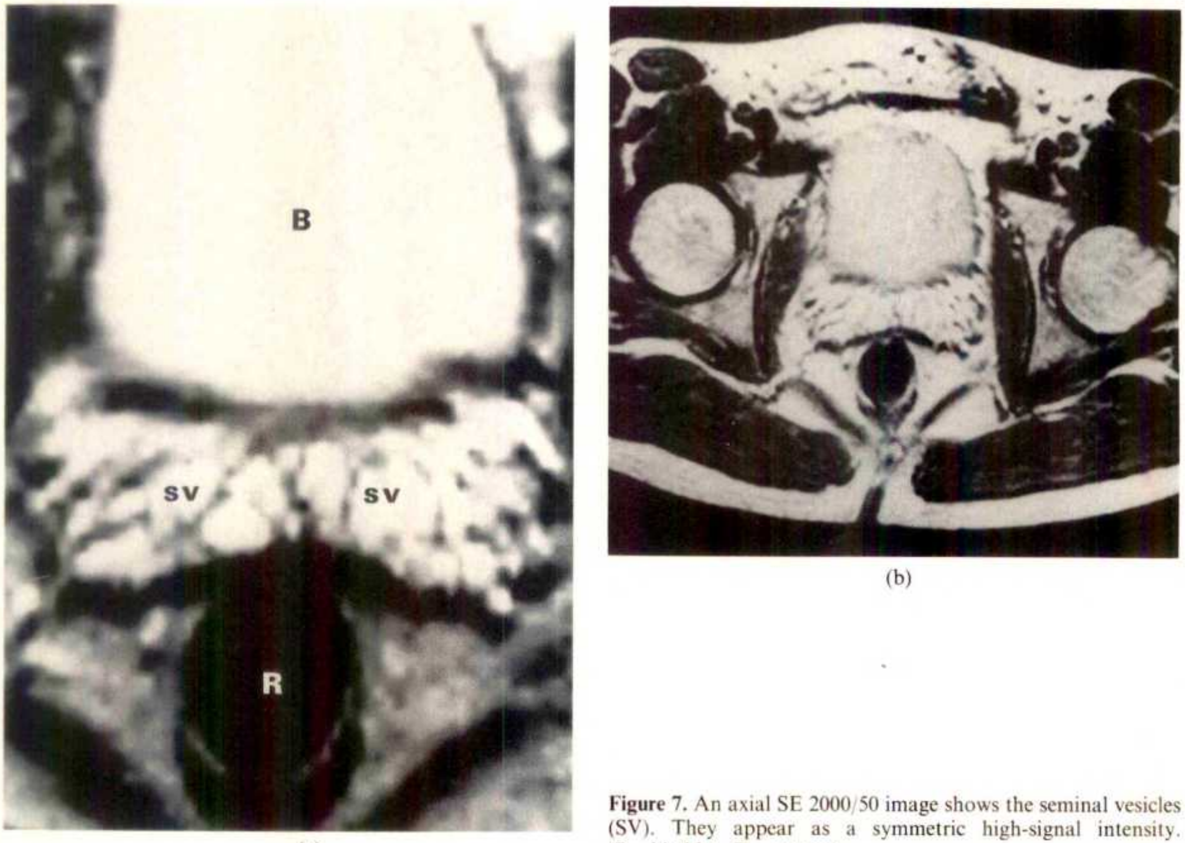
The urethral zone appears as a very high signal. This may result from urine in the urethral lumen or liquid secretions in the periurethral glands within the preprostatic sphincter. The thin, low-signal ring surrounding the urethra may represent this sphincter.

The PVP is always seen. It courses laterally around the prostate to join anteriorly the plexus of Santorini. The plane directly posterior between the prostate and the rectum is known to be avascular. No PVP is ever seen in this region. The high signal of the PVP results from low venous blood flow.

The bulging of the bladder wall is always seen and should not be misinterpreted as tumour infiltration of the inferior wall by prostatic carcinoma.

Seminal vesicles appear as very high symmetrical signals, contrasting with the central prostatic zone. McNeal has shown that the architectural and histologic features of the central zone closely resemble those of the seminal vesicles (McNeal, 1980a), leading to the suggestion that the central zone may be of Wolffian duct origin, while the remainder of the glandular prostate arises from the urogenital sinus. Nevertheless, the intensities of the MR signal from these structures are completely different, reflecting biochemical differences between the structures.

Recent studies have reported the results of MRI of the normal prostate (Sommer et al, 1986; Philips et al,



(a)

(b)

Figure 7. An axial SE 2000/50 image shows the seminal vesicles (SV). They appear as a symmetric high-signal intensity. (B = bladder, R = rectum).

1987a). These retrospective studies have been made with patients aged from 27 to 75 years (Sommer et al, 1986) or from 7 months to 67 years (Philips et al, 1987a), with no clinical evidence of prostatic disease. Berry et al (1984) have observed that the growth of BPH is probably initiated before the patient is 30 years old. The early phase of BPH growth (between 31 and 50 years old) is characterized by the shortest doubling time for the tumour weight (4.5 years). The prevalence of pathological BPH is only 8% at the fourth decade, but 50% of the male population have pathological BPH by the time they are 51–60 years old (Berry et al, 1984). McNeal has emphasized that BPH nodules originate selectively from a very small region near the cylindrical urethral sphincter above the verumontanum, and most nodules arise from the glands and the stroma of the transitional zone of the prostate (McNeal, 1978). Because of this, all 22 of our volunteers were chosen from adults less than 30 years old. Of the supposedly normal specimens examined by other authors, several were probably adenomatous.

Since carcinomas arise frequently in the peripheral zone, any focal disruption of the normal high signal of this zone should arouse suspicion of malignancy. The examination of the prostatic contours and the PVP may be of great interest in the evaluation of extracapsular neoplasic involvement. Although disruption of this high-signal zone can occur in prostatic carcinoma, some authors (Philips et al, 1987b) regard it as an unreliable sign.

References

Berry, S. J., Coffey, D. S., Walsh, P. C. & Ewing, L. L., 1984. The development of human benign prostatic hyperplasia with age. *Journal of Urology*, *132*, 474–479.

Bryan, P. J., Butler, H. E., LiPuma, J. P., Haaga, J. R., El Yoosef, S. J., Resnick, M. I., Cohen, A. M., Malviya, V. K., Nelson, A. D., Clampitt, M., Alfidi, R. J., Cohen, J. & Morrison, S. C., 1983. NMR scanning of the pelvis: initial experience with a 0.3 T system. *American Journal of Roentgenology*, *141*, 1111–1118.

Edwards, C. N., Steinthorsson, E. & Nicholson, D., 1953. An autopsy study of latent prostatic cancer. *Cancer*, *6*, 531–534.

Franks, L. M., 1954. Benign nodular hyperplasia of the prostate; a review. *Annals of Royal College of Surgery*, *14*, 92–106.

Gevenois, P. A., Van Regemorter, G., Van Gansbeke, D., Delcour, C., Corbusier, A. & Struyven, J., 1987a. Pathologie prostatique en résonance magnétique. *Journal de Radiologie*, *68*, 185–192.

GEVENOIS, P. A., GHYSELS, M., CORBUSIER, A., VAN REGEMORTER, G., DEPIERREUX, M. & STRUYVEN, J., 1987b. Leiomyome de la prostate. Aspect en IRM. *Journal de Radiologie, 68*, 631–634.

HRICAK, H., WILLIAMS, R. D., SPRING, D. B., MOON, K. L., HEDGCOCK, M. W., WATSON, R. A. & CROOKS, L. E., 1983. Anatomy and pathology of the male pelvis by magnetic resonance imaging. *American Journal of Roentgenology, 141*, 1101–1110.

MCNEAL, J. E., 1969. Origin and development of carcinoma in the prostate. *Cancer, 23*, 24–34.

MCNEAL, J. E., 1972. The prostate and prostatic urethra: a morphologic synthesis. *Journal of Urology, 107*, 1008–1016.

MCNEAL, J. E., 1978. Origin and evolution of benign prostatic enlargement. *Investigative Urology, 15*, 340–345.

MCNEAL, J. E., 1980a. The anatomy heterogeneity of the prostate. In *Models for Prostate Cancer*. Ed by G. P. Murphy (Alan R. Liss, New York) pp. 149–160.

MCNEAL, J. E., 1980b. Anatomy of the prostate: an historical survey of divergent views. *The Prostate, 1*, 3–13.

PHILIPS, M. E., KRESSEL, H. Y., SPRITZER, C. E., ARGER, P. H., WEIN, A. J., AXEL, L., WARREN, B. G. & POLLACK, H. M., 1987a. Normal prostate and adjacent structures: MR imaging at 1.5 T. *Radiology, 164*, 381–385.

PHILIPS, M. E., KRESSEL, H. Y., SPRITZER, C. E., ARGER, P. H., WEIN, A. J., MARINELLI, D., ASEL, L., GEFTER, W. B. & POLLACK, H. M., 1987b. Prostatic disorders: MR imaging at 1.5 T. *Radiology, 164*, 386–392.

POON, P. Y., MCCALLUM, R. W., HENKELMAN, M. M., BRONSKILL, M. J., SUTCLIFFE, S. B., JEWETT, M. A. S., RIDER, W. D. & BRUCE, A. W., 1985. Magnetic resonance imaging of the prostate. *Radiology, 154*, 143–149.

SOMMER, F. G., MCNEAL, J. E. & CARROL, C. L., 1986. MR depiction of zonal anatomy of the prostate at 1.5 T. *Journal of Computed Assisted Tomography, 10*, 983–989.

1990, *The British Journal of Radiology*, 63, 108–113

Nasopharyngeal carcinoma: the significance of neck node involvement in relation to the pattern of distant failure

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Abstract. The pattern of distant failure of 759 Stage I–IV cases of nasopharyngeal carcinoma was studied. The most common sites of distant metastasis were, in descending order, bone, lung and liver. The N stage, T stage and the characteristics (size and degree of fixation) of the neck nodes involved were found to be significant prognostic factors determining the development of distant metastasis. The bilaterality of neck node involvement, sex, age, haemoglobin and white blood count at diagnosis were not significant. The discriminating effect of N stage holds true in patient groups stratified for the node size and degree of fixation. The superiority of the Ho stage classification was confirmed. The high incidence of distant failure in patients with T_3, N_3, or bulky or fixed neck node involvement warrants further clinical trials to explore the role of adjuvant chemotherapy.

Radiotherapy remains the most important treatment modality for nasopharyngeal carcinoma because of the anatomical constraints and radiosensitivity of this tumour. Recent reviews, however, indicate poor survival despite advances in imaging and radiation therapy machines and techniques. One of the important causes of failure is distant metastasis (Huang, 1980; Qin et al, 1988). As radiotherapy is a locoregional form of treatment, improvement in survival rates for patients with high risk of distant failure is not expected when reliance is entirely on radiotherapy. We have reviewed our experience on the pattern of distant failure with special reference to the pattern of neck node involvement and have tried to identify prognostic factors predictive of distant failures.

Patients and methods

From 1976 to 1983, 841 patients with newly diagnosed nasopharyngeal carcinoma were referred to our department. Thirty-seven of them had distant metastasis (Stage V disease) and were not given radical radiotherapy. Another 45 patients either refused treatment or died from advanced disease before the completion of radiotherapy. These 82 patients were excluded from the present analysis. The remaining 759 Stage I–IV patients formed the basis of the present study.

There were 561 male and 198 female patients. Their age ranged from 15 to 83 years with a median age of 49. All patients had histological confirmation by biopsy of the primary tumour in the nasopharynx: 427 (56.3%) of the tumours were classified as undifferentiated carcinoma; 283 (37.3%) as poorly differentiated squamous carcinoma; 31 (4.0%) were not subclassified and only 16 (2.1%) and 2 (0.3%) respectively were classified as moderately and well differentiated squamous carcinoma.

All patients were staged according to Ho's classification system (Ho, 1970). The T_1 tumours are those confined to the nasopharynx; T_2 tumours are those extending to the nasal fossa, oropharynx, and adjacent muscles and nerves below the base of skull and T_3 tumours are those extending beyond the T_2 limit. For N stage grouping, the neck is divided into three regions by the skin crease extending from the laryngeal eminence laterally, and the line joining the upper margin of the sternal end of the clavicle and the apex of an angle formed by the lateral surface of the neck and the superior margin of the trapezius. Patients with no clinically palpable neck nodes are staged as N_0. When the lowest lying node involved the uppermost, middle and the lowest regions of the neck, the patient was staged N_1, N_2 and N_3 respectively. Bilateral nodal involvement does not influence the N stage.

All patients were examined carefully at presentation for cervical lymphadenopathy; the position of the nodes in relation to the three levels of the neck, dimension of the nodes and the degree of fixation were noted and documented by line drawings. In addition to general examination, special care was taken to identify oropharyngeal and nasal extension of the disease and cranial nerve palsies. Clinical examination was complemented by chest radiograph, liver function test and the standard five views of the nasopharynx which are particularly useful for the detection of tumour invasion of the base of skull (Ho, 1967).

Six hundred and sixty-nine patients were treated with cobalt 60 or linear accelerator using the techniques described by Ho (Ho, 1982); 290 (38.2%) of them were treated by split field technique with two lateral opposing facial fields and one anterior facial field. A central tumour dose of 3.5 Gy or 3.8 Gy per fraction was given three times a week, aiming at a total of 53.2 Gy to 59.5 Gy. Three hundred and seventy-nine patients

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Table I. T and N stage distribution

	T_1	T_2	T_3	Subtotal
N_0	72	5	49	126
N_1	149	8	60	217
N_2	153	13	42	208
N_3	123	29	56	208
Subtotal	497	55	207	

Table III. First and subsequent sites of failure

	Number of patients
Nasopharynx or neck nodes	302
No subsequent distant failure	209
Subsequent distant failure	93
Distant failure	183
No subsequent locoregional failure	160
Subsequent locoregional failure	23

(49.9%) were treated with lateral opposing faciocervical fields for the initial phase of treatment; a midplane tumour dose of 2.5 Gy per fraction was given four times a week to 40 Gy. Phase two treatment was given by split field technique with two lateral opposing facial fields and one anterior facial field, a central tumour dose of 3.5 Gy or 3.8 Gy per fraction being given three times a week aiming at another 14 to 21 Gy.

Ninety patients (11.9%) were treated by kilovoltage machine with two anterior oblique and two posterior oblique fields: 1.5 Gy was given daily to 30 Gy. This was followed by 3.5 Gy or 3.8 Gy per fraction given three times a week aiming at another 30.4 Gy to 31.5 Gy. Most of these patients were treated in the earlier period and had bulky neck node involvement.

Therapeutic neck treatment was given to patients with neck node metastasis, and prophylactic neck treatment was given for those with no clinically palpable nodes. The technique and dose were the same for all patients: both sides of neck from the level of mastoid to just above the supraclavicular fossae were treated, aiming at a dose ranging from 45.6 Gy/12 fractions/4 weeks to 54 Gy/20 fractions/5.5 weeks.

After completion of radiotherapy all patients were followed up every 4 to 6 weeks for the first year, then every 2 months for the second year and every 3 months for the third year. The time interval between follow-ups was then gradually increased to every half year and follow-ups were continued indefinitely. At each visit the nasopharynx, the neck and the abdomen were carefully examined. Chest radiograph was performed yearly. Other radiological and blood tests were done when clinical symptoms and signs indicated the need.

The median follow-up duration for the whole group of patients was 64 months and the maximum was 149 months; 44 patients were lost from follow-up, and 26 of them had been followed-up for more than two years when last seen.

The risk factors for distant failure were determined by regression analysis with covariates using Cox's models (Cox, 1972). The risk of distant failure for patients stratified for different stage, N stage, T stage, and characteristics of node involvement, were computed by the Kaplan–Meier method (Kaplan & Meier, 1958) and the difference between curves tested by the Mantel–Cox test (Mantel & Haenszel, 1959). Computations were performed by the BMDP Statistical Software.

Results

The stage distribution of these patients was: 72 (9.5%), Stage I; 162 (21.3%), Stage II; 317 (41.8%), Stage III and 208 (27.4%), Stage IV. The number of patients with N_0, N_1, N_2 and N_3 disease were 126 (16.6%), 217 (28.6%), 208 (27.4%) and 208 (27.4%) respectively. Of the patients with neck node metastasis, 274 (43.3%) had bilateral involvement. The number of patients with T_1, T_2 and T_3 disease were 497 (65.5%), 55 (7.2%) and 207 (27.3%) respectively. The T and N stage distribution of patients are shown in Table I. There was no linear correlation between the T stage and the N stage ($p = 0.22$).

Patients with cervical lymphadenopathy were grouped into three types according to the size and degree of fixation of the nodes (Table II). Type 1 consisted of patients with mobile nodes less than 4 cm in diameter (310/633, 49.0%). Type 2 consisted of patients with nodes between 4 cm and 6 cm or partially fixed nodes (200/633, 31.6%). Type 3 consisted of patients with nodes 6 cm or greater or fixed nodes (123/633, 19.4%).

Table II. Classification of neck node involvement by size and degree of fixation

		Number of patients
Type 1	All nodes are mobile and the largest one less than 4 cm (greatest diameter)	310
Type 2	Any node between 4 cm and 6 cm, or partially fixed	200
Type 3	Any node 6 cm and greater or fixed	123

Table IV. Site of distant metastasis

	Number of patients with this as first site of failure	Total number of patients with this site ultimately involved
Bone	84	153
Lung	56	102
Liver	29	72
Others	14	27

Table V. Multivariate analysis for prognostic factors influencing distant metastasis

Factors	Category or unit	Coefficient	p
N Stage	0 I, II and III	0.3933	<0.0001
Type of node involvement	0, 1, 2 and 3	0.2184	0.0110
T stage	I, II and III	0.2880	<0.0001
Bilaterality of nodes	Unilateral or bilateral		0.5232
Sex	Male or female		0.2410
Age	years		0.7856
Haemoglobin	g/dl		0.6087
White cell count	10^9/l		0.7152

Table VI. Incidence of distant metastasis by stage, N stage and T stage by the end of the first, second and fifth years

		First year		Second year		Fifth year	
Stage	I	1/72	1.4%	5/72	6.9%	8/72	11.1%
	II	10/162	6.2%	22/162	13.6%	32/162	19.8%
	III	50/317	15.8%	85/317	26.8%	114/317	36.0%
	IV	74/208	35.6%	95/208	45.7%	110/208	52.9%
N Stage	0	7/126	5.6%	22/216	17.5%	28/126	22.2%
	1	17/217	7.8%	30/217	13.8%	44/217	20.3%
	2	37/208	17.8%	60/208	28.8%	82/208	39.4%
	3	74/208	35.6%	95/208	45.7%	110/208	52.9%
T Stage	1	78/497	15.7%	120/497	24.1%	154/497	31.0%
	2	18/55	32.7%	26/55	47.3%	28/55	50.9%
	3	39/207	18.8%	61/207	29.5%	82/207	39.6%

Three hundred and two (39.7%) patients relapsed locally in the nasopharynx or regionally in neck node; 93 of them subsequently developed distant metastasis. One hundred and eighty-three patients (24.1%) developed distant metastasis as the first site of failure. All in all, 276 (36.4%) patients, at one time or another, failed distantly (Table III).

The most common distant failure sites were bone, lung, and liver respectively (Table IV).

By Cox's multivariate analysis the N stage, T stage and the type of neck node involvement were the significant prognostic factors determining the development of distant metastasis (Table V), whereas bilaterality of neck node involvement, sex, age, haemoglobin and white cell count at diagnosis were not significant. The risk of developing distant metastasis for patients with different stages, N and T stages and types of neck node involvement are shown in Figs 1–4 and the difference in each is significant ($p<0.0001$). However, the difference between T_2 and T_3 in Fig. 3 was not significant ($p=0.37$). The number of distant failures at the end of the first, second and fifth years are shown in Table VI.

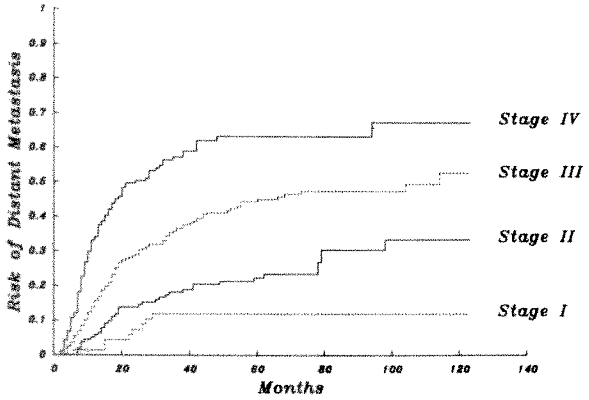

Figure 1. Risk of distant failure by stage ($p<0.0001$).

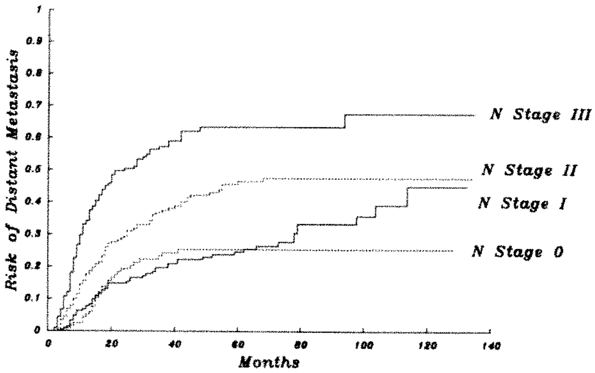

Figure 2. Risk of distant failure by N stage ($p<0.0001$).

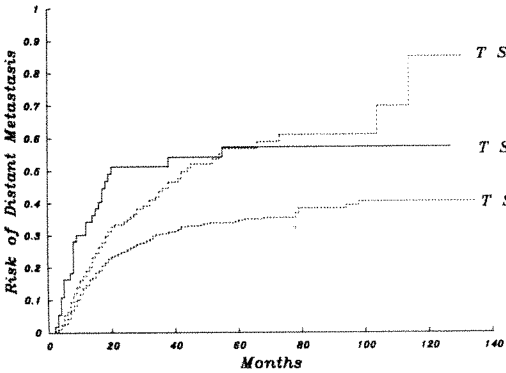

Figure 3. Risk of distant failure by T stage ($p<0.0001$).

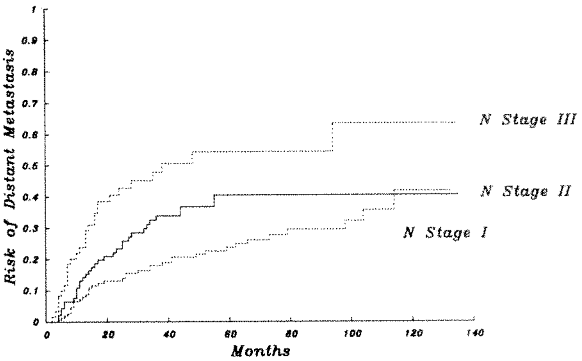

Figure 5. Risk of distant failure by N stage for patients with Type 1 node involvement ($p=0.0001$).

The discriminating power of N stage in predicting distant metastasis holds true in patient groups stratified for node characteristics. Among patients with Type 1 and 2 node involvement, the differences were significant ($p=0.0001$ and $p=0.0013$ respectively, Figs 5 and 6). For patients with nodes fixed or more than 6 cm in diameter (Type 3), the chance of distant metastasis was uniformly high (Fig. 7).

Discussion

The incidence of 36.4% distant metastasis in the present series is comparable to some of those reported in the literature (Marcial et al, 1980; Mesic et al, 1981; Qin et al, 1988), but appears to be more frequent than some other series which reported 15.8% to 21.9% (Moench & Phillips, 1972; Hoppe et al, 1976; Schabinger et al, 1985). Strict comparison is not possible because of the difference in stage distribution and stage classification used. In addition to stage distribution and the possible difference in natural history of this tumour in different racial groups, another possible explanation for this higher incidence of distant metastasis in the present series is the histology: 56.3% of our patients had undifferentiated carcinoma. The reported incidence of distant metastasis for lymphoepithelioma was higher than squamous carcinoma (35.4% and 23% respectively) (Mesic et al, 1981).

In contrast to data of Bedwinek et al (1980) and Mesic et al (1981), who reported a close association between N stage but not T stage and distant metastasis, our data suggests that the incidence of distant metastasis is correlated with the T stage, N stage and the characteristics of the cervical nodes, although there was no correlation with bilaterality of neck node involvement.

The parameters underlying the N stage classification adopted by Bedwinek et al (1980) and Mesic et al (1981) are the size of the nodes and contralateral neck involvement (American Joint Committee for Cancer Staging and End Result Reporting, 1978). This is similar to the stage classification of other head and neck tumours. The importance of the node size was embodied in our classification of node involvement, and we have shown that it was positively correlated with distant failure, although we found bilateral involvement to be of no significance. We have, however, confirmed that the Ho stage classification of N stage is superior in that it discriminates even among patient groups stratified by the size of the nodes.

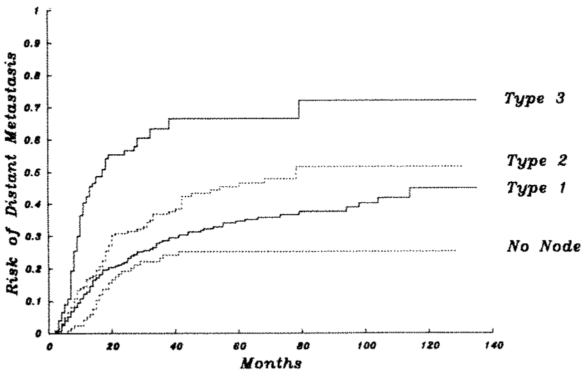

Figure 4. Risk of distant failure by type of node involvement ($p<0.0001$).

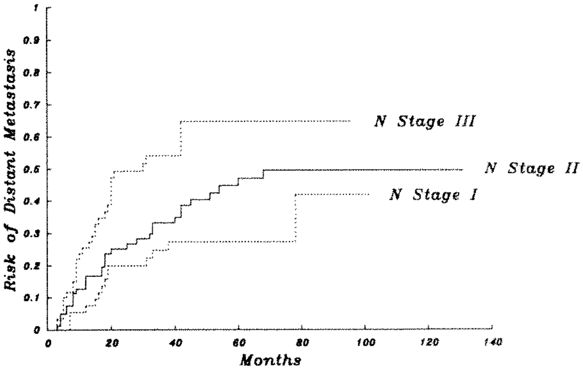

Figure 6. Risk of distant failure by N stage for patients with Type 2 node involvement ($p=0.0013$).

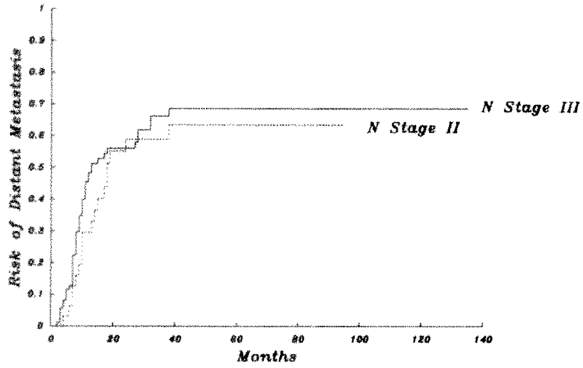

Figure 7. Risk of distant failure by N stage for patients with Type 3 node involvement ($p = 0.60$).

It is unfortunate that this classification has not been widely used (Fu, 1980).

The superiority of the Ho stage classification is supported by sound pathological studies. Nasopharyngeal carcinoma has a high propensity for lymph node metastasis compared with other head and neck tumours. It is centrally situated in the head, often with bilateral cervical node involvement; most of the time the first clinically palpable nodes are in the high cervical chain and then spread downwards (Ho, 1978). For other unilaterally situated tumours like carcinoma of tonsil, the significance of contralateral neck involvement will obviously be prognostically more important than in the case of nasopharyngeal carcinoma.

For tumour like that of the hypopharynx, the first clinical node involvement is often in the mid-neck, its next site of involvement can be nodes higher up or further down the neck. In the case of nasopharyngeal carcinoma, we have the opportunity of assessing the degree of spread from the high cervical chain downwards to the supraclavicular fossae. By dividing the neck into three regions, and ranking the involvement from above downwards, it is hoped that the ranking will measure the propensity for spread and the actual extent of spread via the lymphatics. It is also hoped that such a measure of spread via the lymphatics will be useful as an indicator of distant metastasis.

It is interesting to note that there was no significant difference between T_2 and T_3 patients as far as the distant metastasis is concerned. This lack of difference may reflect the inadequacy of clinical examination in detecting parapharyngeal, nasal and oropharyngeal extension of tumour without the use of computed tomography (Yu et al, 1985). The tumour which has clinically evident extension to these sites can be more extensive than a tumour with early invasion of the cavernous sinus and impinged on the sixth cranial nerve.

As radiotherapy is a locoregional form of treatment, improvement in survival rates for patients with high risk of distant failure is not expected when reliance is entirely on radiotherapy. The treatment strategy for this group of patients should include emphasis on the eradication of possible occult metastasis by adjuvant chemotherapy. Even though the result of adjuvant chemotherapy for nasopharyngeal carcinoma has been disappointing and the late toxicity was not slight (Tannock et al, 1987; Peters et al, 1988), the high incidence of distant metastasis warrants further clinical trials in this direction. Patients at very high risk of such failure, for example those with bulky or fixed nodes, N_3 or T_3 disease, should be recruited into properly controlled randomized trials of combined radio-chemotherapy.

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References

AMERICAN JOINT COMMITTEE FOR CANCER STAGING AND END RESULT REPORTING, 1978. *Manual for Staging of Cancer* (AJCCSERR, Chicago).

BEDWINEK, J. M., PEREZ, C. A. & KEYS, D. J., 1980. Analysis of failures after definitive irradiation of epidermoid carcinoma of the nasopharynx. *Cancer, 45*, 2725–2729.

COX, D. R., 1972. Regression models and life tables. *Journal of Royal Statistics Society, Series B, 34*, 187–220.

FU, K. K., 1980. Prognostic factors of carcinoma of the nasopharynx. *International Journal of Radiation Oncology, Biology, Physics, 6*, 523–526.

HO, J. H. C., 1967. Radiological diagnosis of nasopharyngeal carcinoma with special reference to its spread through the base of skull. In *Nasopharyngeal Cancer UICC Monograph Series*, Vol. 1. Ed. by C. S. Muir & K. Shanmugaratnam (Medical Examination Publications, New York), pp. 238–246.

HO, J. H. C., 1970. The natural history and treatment of nasopharyngeal carcinoma (NPC). In *Oncology* (Proceedings of the 10th International Cancer Congress, Vol. 4). Ed. by R. Lee-Clark, R. W. Cumley, J. E. McKay & M. Copeland (Year Book Medical Publishers, Chicago), pp. 1–14.

HO, J. H. C., 1978. An epidemiologic and clinical study of nasopharyngeal carcinoma. *International Journal of Radiation Oncology, Biology, Physics, 4*, 183–198.

HO, J. H. C., 1982. Nasopharynx. In *Treatment of Cancer*. Ed. by K. E. Halnan (Chapman and Hall, London), pp. 249–267.

HOPPE, R. T., GOFFINET, D. R. & BAGSHAW, M. A., 1976. Carcinoma of the nasopharynx, eighteen years' experience with megavoltage radiation therapy. *Cancer, 37*, 2605–2612.

HUANG, S. C., 1980. Nasopharyngeal cancer: a review of 1605 patients treated radically with cobalt 60. *International Journal of Radiation Oncology, Biology, Physics, 6*, 401–407.

KAPLAN, E. L. & MEIER, P., 1958. Nonparametric estimation from incomplete observations. *Journal of American Statistics Association, 53*, 457–481.

MANTEL, N. & HAENSZEL, W., 1959. Statistical aspects of the analysis of data from retrospective studies of disease. *Journal of National Cancer Institute, 22*, 719–748.

MARCIAL, V. A., HANLEY, J. A., CHANG, C., DAVIS, L. W. & MOSCOL, J. A., 1980. Split-course radiation therapy of carcinoma of the nasopharynx: result of a National Collaborative Clinical Trial of the Radiation Therapy Oncology Group. *International Journal of Radiation Oncology, Biology, Physics, 6*, 409–414.

MESIC, J. B., FLETCHER, G. H. & GOEPFERT, H., 1981. Megavoltage irradiation of epithelial tumors of the nasopharynx. *International Journal of Radiation Oncology, Biology, Physics, 7*, 447–453.

MOENCH, H. C. & PHILLIPS, T. L., 1972. Carcinoma of the nasopharynx, review of 146 patients with emphasis on radiation dose and time factor. *American Journal of Surgery, 124,* 515–518.

PETERS, L. J., HARRISON, M. L. & DIMERY, I. W., 1988. Acute and late toxicity associated with sequential bleomycin-containing chemotherapy regimens and radiation therapy in the treatment of carcinoma of the nasopharynx. *International Journal of Radiation Oncology, Biology, Physics, 14,* 623–633.

QIN, D., HU, Y., YAN, J., XU, G., CAI, W., WU, X., CAO, D. & GU, X., 1988. Analysis of 1379 patients with nasopharyngeal carcinoma treated by radiation. *Cancer, 61,* 1117–1124.

SCHABINGER, P. R., REDDY, S., HENDRICKSON, F. R., PHILLIPS, R. L. & SAXENA, V., 1985. Carcinoma of the nasopharynx: survival and patterns of recurrence. *International Journal of Radiation Oncology, Biology, Physics, 11,* 2081–2084.

TANNOCK, I., PAYNE, D., CUMMINGS, B., HEWITT, K. & PANZARELLA, T., 1987. Sequential chemotherapy and radiation for nasopharyngeal cancer: absence of long-term benefit despite a high rate of tumor response to chemotherapy. *Journal of Clinical Oncology, 5,* 629–634.

YU, Z. H., XU, G. Z., HUANG, Y. R., HU, Y. H., SU, X. G. & GU, X. Z., 1985. Value of computed tomography in staging the primary lesion (T-staging) of nasopharyngeal carcinoma (NPC): an analysis of 54 patients with special reference to the parapharyngeal space. *International Journal of Radiation Oncology, Biology, Physics, 11,* 2143–2147.

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Radiobiological rationale for compensation for gaps in radiotherapy regimes by post-gap acceleration of fractionation

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Abstract. It is now recognized that clonogenic tumour cells may repopulate vigorously during radiotherapy. Gaps in treatment schedules which lead to prolongation of overall treatment time may therefore cause sparing of tumour. Acute-responding normal tissues will also be spared if repopulation by surviving stem cells takes place. However, it is unlikely that stem cells in late-responding normal tissues repopulate significantly over the time-scale of a conventional treatment regime; these tissues will therefore experience little or no sparing as a result of a gap. This poses a dilemma since tumour cell repopulation implies that an increased therapeutic effect in the post-gap phase of treatment may be necessary to compensate for any prolongation of treatment time, but it is difficult to achieve increased tumour effect without also increasing damage to late-responding normal tissues. Neither increased total dose nor increased fraction size is able to achieve this. A possible solution is provided if total treatment time can be held constant, with unchanged total dose and fraction size, by use of twice-daily conventionally sized dose fractions administered after the gap. Provided the twice-daily fractions are sufficiently spaced (not less than 6–8 h apart), the result will be to offset repopulation in tumour and acute-responding normal tissues without additional impairment of late-responding normal tissues. The feasibility of the approach depends on being able to complete treatment by the time originally intended; it is therefore more readily applicable to gaps occurring early rather than late in a treatment schedule. The strategy should be especially advantageous for tumours with rapid repopulative potential in sites where risk of damage to late-responding normal tissues imposes limitation of dose.

In recent years, split-course radiotherapy regimes with a gap between two phases of conventionally fractionated treatment have become less popular. This is because of evidence of reduced therapeutic differential for regimes involving prolongation of total time and because of indirect kinetic evidence of rapid repopulation of surviving tumour cells during a course of treatment (Withers et al, 1988). Unplanned gaps, however, still occur. These may arise for two reasons. Firstly, an initially unintended gap may be imposed for clinical reasons, for example where a patient shows an unexpectedly severe mucosal reaction which must be allowed to decrease before treatment can be resumed. Secondly, gaps may occur for a variety of reasons unrelated to radiation reactions: these include patient illness, machine breakdown and public holidays.

In the case of gaps in the first category, the continuation of the regime must be managed empirically. The total dose given will depend on what mucosal reactions will permit, and this will have to be reviewed throughout treatment. The second group of reasons for gaps pose a clinical dilemma of a different kind. Since the gap has not been forced by untoward radiation reactions, and evidence exists that time prolongation may reduce tumour curability, there is an implication that some form of compensation for the gap is required. What should this be? In practice, clinical strategies that are used include neglect of the gap, increased number of fractions and total dose or increased dose per fraction. The purpose of this paper is to draw attention to an alternative strategy: post-gap acceleration of fractionation, which may be advantageous.

Repopulation in normal tissues and tumours

It has long been known that prolongation of overall time, either by introduction of a gap, or by wider spacing of treatment fractions in a uniform regime, has a sparing effect (for given total dose) on acute-responding tissues such as epidermis, gastrointestinal tract and oral mucosa and haemopoietic tissues. This is probably because of repopulation by surviving clonogenic cells. Evidence exists (Turesson & Notter, 1984) that basal cell repopulation in epidermis begins approximately 4 weeks after the start of treatment and is rapid thereafter. It is likely that other acute-responding tissues behave similarly, though with a tissue-specific time of onset of repopulation.

Some attempts have been made to quantify the sparing effects of repopulation for acute-responding tissues by power-law isoeffect formulae of the nominal standard dose type (Ellis, 1969; Kirk et al, 1971; Orton & Ellis, 1973). However, it seems most unlikely that the mathematical form of power-functions is appropriate for doing this, and the corrections for time protraction predicted by these models are probably in error (Fowler, 1984). Similar attempts to incorporate a time-factor in the linear quadratic model run into difficulties such as the need to measure α and β values individually (rather than the α/β ratio) as well as the relevant kinetic factors (Wheldon & Amin, 1988). The current status of the time-dependent formulation of the linear quadratic model has been included in the recent review by Fowler (1989). At present, it seems doubtful whether time factors are sufficiently well known to enable their clinical application. Although time protraction will usually result in some sparing of acute-responding normal tissues, quantitation of this remains unreliable.

In contrast, it is likely that late-responding normal tissues are little spared by time prolongation within the time scales of conventional radiotherapy (Thames & Hendry, 1987; Hall, 1988). Theoretically, a prompt response of repopulation in late-responding tissues is not expected (Michalowski, 1981). It is possible that lung may be an exception in that time prolongation over a scale of weeks does seemingly result in modest sparing; this is attributed to the poorly understood phenomenon of "slow repair", but this has not been seen in other late-responding organs (Field et al, 1976). Since late-responding tissues are usually dose-limiting in radiotherapy, and repopulation probably does not occur during a typical course, it seems unlikely that gaps of only a few days would enable higher doses of radiation to be given without increased risk of tissue injury.

In the case of tumours, the recognition of high repopulative capacity in those which are slowly growing at the start of therapy has been an important development. Analysis of reduced therapeutic benefit in prolonged or split-course regimes has provided evidence for actual doubling times of surviving clonogenic cells which are typically of the order of a few days (Thames & Hendry, 1987, pp. 124–127). Indirect evidence supports a proportionality relationship between recurrence time of irradiated tumours and the cell kinetic potential doubling time (Trott & Kummermehr, 1985) which may be a predictive parameter for tumours with high repopulative capacity. Potential doubling times of 3 or 4 days have been reported in several tumour types (Trott & Kummermehr, 1985) and as short as approximately 1–2 days in nephroblastoma (Aherne & Buck, 1971). Also, the potential doubling time may underestimate repopulation since an expansion of the clonogenic growth fraction (taken to be constant in calculations of potential doubling time) occurs in experimental tumours (Steel, 1977) and seems plausible for human tumours.

These considerations have given rise to interest in the use of time-shortened (accelerated) treatment schedules as a means of improving the radiotherapy of at least some tumour types (Thames et al, 1983). The same considerations suggest that gaps of some days' duration are not necessarily negligible and that significant tumour repopulation might occur if remedial action is not taken.

Neglect of gaps

If a gap is simply neglected, the radiotherapy regime resumes when possible and ends at the same total dose level originally intended. The net effect will be that the total dose is delivered over an increased total time. The effects on normal tissues will be sparing of acute-responding tissues with negligible effects on late-responding tissues.

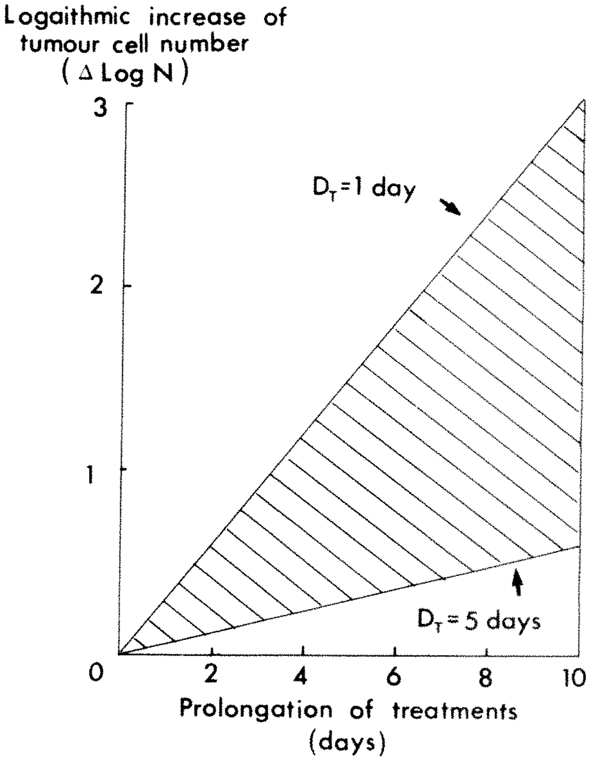


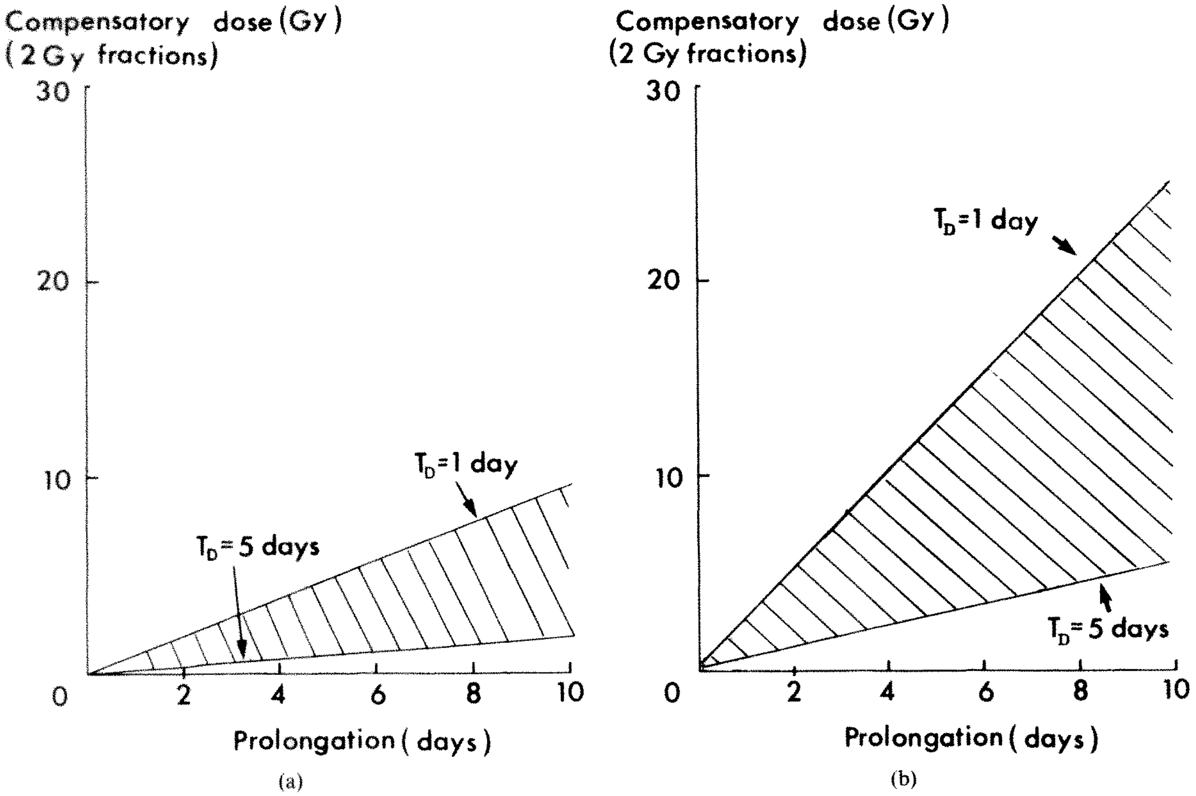
Figure 1. Estimated change in tumour cell number (Δ log N) expected to result from treatment prolongation for tumour doubling times in the range 1–5 days.

However, it is the possible sparing of tumours that gives rise to concern. This will, of course, vary from one tumour to another in accordance with its radiobiological and kinetic properties.

Some idea of the importance of gaps in terms of tumour repopulation is given by Fig. 1, which shows the net increase of tumour cell number, for doubling times in the range 1–5 days, as a function of the magnitude of prolongation of the treatment regime resulting from the gap. It is worth noticing that this calculation does not require the tumour cells to be proliferating at this rate *during* the gap. The importance of the gap is that it prolongs overall treatment time. If increased tumour cell proliferation takes place as a result of prolongation (for example starting after the gap) then prolongation will reduce the net effect of treatment on the tumour. Significant increases of tumour cell number could be facilitated by gaps of only a few days. The implication is that such gaps cannot be neglected without increased risk of tumour recurrence.

Compensation by increased total dose

A possible strategy of gap compensation is to give additional treatment *i.e.* by adding conventionally sized



(a) (b)

Figure 2. Estimated dose (given as 2 Gy fractions) to compensate for tumour proliferation during treatment prolongation for doubling times in the range 1–5 days for (a) radiosensitive tumour cell populations ($S_2=0.22$) and (b) radioresistant tumour cell population ($S_2=0.58$). The S_2 values are those given by Fertil and Malaise (1985) as the mean for the most sensitive and the most resistant of six groups of tumour cell lines ranked for radiosensitivity *in vitro*. It should be noted that doses to compensate for tumour proliferation will not necessarily result in equal effects on normal tissues.

treatment fractions. There is however, a two-fold difficulty. First, little sparing of late-responding tissues is likely to have resulted from the gap. If the originally intended treatment came close to tolerance for late-responding tissues, there may be no safe margin for further increase of dose. Secondly, the additional dose which should be given to compensate for tumour repopulation will depend on tumour survival curve parameters as well as repopulation kinetics and will vary not only from one tumour type to another but from patient to patient.

Some idea of the magnitude of compensatory dose increments required for gaps may be gained by a calculation which makes use of the *in vitro* tumour radiosensitivity data of Fertil and Malaise (1985). These authors summarized data on a large number of human tumour cell lines, dividing these into six categories, ranked for radiosensitivity. Conveniently, cell line radiosensitivity may be represented by the S_2 value: the surviving fraction following a 2 Gy radiation dose. Fertil and Malaise reported that the most resistant group has a mean S_2 value of 0.58 and the most sensitive group a mean S_2 value of 0.22. The compensatory dose (given as 2 Gy fractions) has been calculated for the most resistant and most sensitive groups, for doubling times ranging from 1–5 days, as a function of prolongation caused by a gap. Figure 2 shows the results of these calculations and demonstrates the wide range of compensatory doses that would be required. This form of compensation is accompanied by the difficulty of knowing whether the dose compensation used is appropriate for the individual tumour, and whether there will be an increased risk of injury to late-responding tissues.

Compensation by increased dose per fraction

A related strategy is to increase fraction size in the post-gap phase of treatment to keep overall treatment time the same. This has the merit that no estimation of tumour repopulation seems to be required: since the overall treatment time remains the same, the contribution to net tumour survival made by repopulation will be unchanged. The problem is that if the gap provides no sparing of late-responding tissues, these tissues will experience greater damage than originally intended if fraction size is increased without change of total of dose.

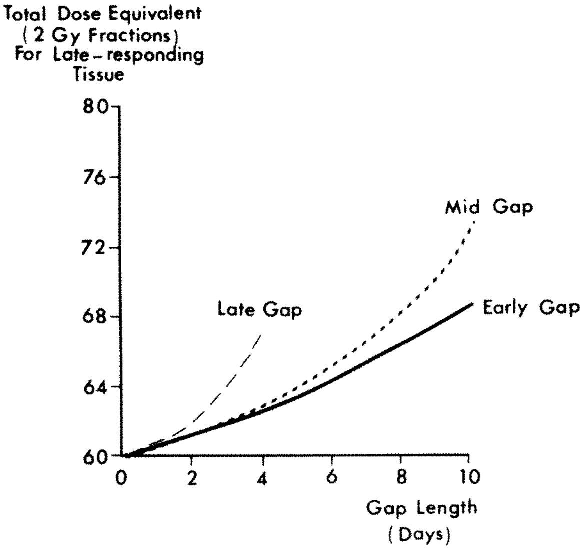


Figure 3. The diagram depicts the biological effect on late-responding normal tissues (expressed as equivalent total dose given as 2 Gy fractions) which would result from attempting to compensate for gaps of varying size, occurring at three different positions in the schedule, by the strategy of increased fraction size. The schedule originally intended was taken to be 30 × 2 Gy over 6 weeks. Gap position was defined as at 1 week (early stage), 3 weeks (mid-stage) or 5 weeks (late stage) after the commencement of therapy. The number of fractions in the compensatory post-gap phase of treatment was taken to be the number of treatment days remaining within the 6 week period and the fraction size was chosen such that the composite regime should have the same effect on a typical tumour (α/β = 20 Gy on the linear quadratic model) as the originally intended regime (Table I). The calculation of equivalent total dose (given as 2 Gy fractions) for damage to late-responding normal tissues used the linear quadratic model with $\alpha/\beta = 3$ Gy.

Table I. Treatment schedules incorporating increased fraction size following a gap to give unchanged treatment time and unchanged radiobiological effect on typical tumour

Duration of gap (days)	Post-gap phase of treatment schedule		
	Early stage gap	Mid-stage gap	Late stage gap
2	23 × 2.16 Gy	13 × 2.28 Gy	3 × 3.17 Gy
4	21 × 2.34 Gy	11 × 2.65 Gy	1 × 7.89 Gy
6	19 × 2.57 Gy	9 × 3.17 Gy	—
8	17 × 2.84 Gy	7 × 3.94 Gy	—
10	15 × 3.17 Gy	5 × 5.23 Gy	—

Notes.

(1) The originally intended regime (without gaps) was taken to be 30 × 2 Gy in 6 weeks.

(2) Gap position was defined as follows: early stage—gap commencing after 1 week of therapy (5 × 2 Gy given); mid-stage—gap commencing after 3 weeks of therapy (15 × 2 Gy given) and late stage—gap commencing after 5 weeks of therapy (25 × 2 Gy given).

(3) Fraction number in the post-gap phase was taken to be the number of treatment days remaining (within the 6 week time period originally intended) following the gap. For the late stage gap, with gap duration > 5 days, the 6 week period is exceeded by the gap; hence this procedure cannot be used to give unchanged treatment time and unchanged effect on tumour.

(4) Fraction size in the post-gap phase was calculated from the linear quadratic model with $\alpha/\beta = 20$ Gy ("typical" value for a tumour) such that the post-gap phase, together with treatment already given, should have equivalent tumour effect to the originally intended regime.

The magnitude of this effect varies from one situation to another but may be illustrated by some examples. Consider the situation in which a conventional radical regime (30 × 2 Gy, 6 weeks) is interrupted by a gap of variable length which can occur anywhere within the schedule. Specifically, we shall consider an early stage gap (after the first week of therapy), a mid-stage gap (after the third week of therapy) and a late stage gap (after the fifth week of therapy). In each case, suppose the fraction size of remaining treatments is increased to keep overall time the same and the radiobiological effect on the tumour as originally intended. The choice of fraction size, if radiobiological effects on the tumour are to be unchanged, requires knowledge of the radiobiological properties of each individual tumour. For example, if the linear quadratic model is used to calculate iso-effective doses, the α/β ratio for the tumour must be known. Usually, this information will not be available. However, studies of experimental tumours have suggested that an α/β ratio of approximately 20 Gy may be typical, at least for murine tumours, although considerable variation is seen (Williams et al, 1985). Adopting this as a representative value, it is theoretically possible to compute fraction size increases that just compensate for the occurrence of the gap in terms of effects on the tumour.

Table I shows how the regimen would have to be modified in its post-gap phase to give equal effects on the tumour. Unfortunately, the effect on late-responding normal tissues is no longer the same. This phenomenon is illustrated in Fig. 3, which shows how the resultant biological effect on late-responding tissue increases with gap length for each of the three gap positions considered. The effect on late-responding normal tissues is expressed in terms of a "conventional schedule equivalent", *i.e.* the total dose (given as 2 Gy fractions) which would have the same effect on the tissue concerned as the actual regime. These results show that the biological effects on late-responding normal tissues would be greater than originally intended (60 Gy as 2 Gy fractions). This shows that appropriate compensation, to give the same effects as originally intended on both tumour and late-responding tissues, is not possible even if the relevant α/β ratio values are all known. The strategy of increased fraction size cannot therefore provide a satisfactory solution to the problem of gap compensation.

General equivalence

The time gap problem is a special case of the problem of "general equivalence" *i.e.* the conditions under which two schedules of differing fractionation structure can have identical effects on all tissues irradiated. Recently, Deehan and O'Donoghue (1988) have discussed the conditions for general equivalence of two schedules which are given in the same overall time. Here, the problem is to derive schedule parameters such that a sequence of two (or more) fractionated schedules are simultaneously equivalent for *all* tissues to a particular uniform schedule (*i.e.* independent of α/β ratios). In the circumstances described in this paper, we have the degenerate case where the "intended" schedule and the schedule already given have the same fraction size. The equations for general equivalence have the solutions such that:

1. The schedule remaining to be given must also have the same fraction size.
2. It must have the number of fractions that is the difference between the intended schedule and the schedule already given.

If the schedule remaining to be given has any other fraction size or fraction number, general equivalence is impossible and the best that can be achieved is an equivalence for only one value of α/β. This means that general equivalence between the originally intended schedule and the schedule including a time-gap usually cannot be achieved by increased total dose or dose per fraction.

Rationale for post-gap acceleration

The above considerations lead to disappointing conclusions in terms of compensating for gaps. A difficulty with some compensation strategies is that they attempt a "trade-off" between time and dose or dose per fraction. Even if all the relevant radiobiological parameters are known, this trade-off differs between normal tissues and tumours making any dose compensation strategies incapable of achieving the same overall effects as the originally intended schedule.

An alternative approach is to try to keep the overall time constant, despite the gap, but without changing either dose or dose per fraction. Simply, fractions would be given more frequently after the gap than before it *i.e.* the post-gap phase of treatment would be accelerated, though the regimen as a whole would not. This could be done by giving two rather than one conventionally sized fractions daily following the gap for as many days as is necessary to ensure total time remains constant. Current evidence implies that an interval of at least 6 h (and preferably more) should be allowed between any two fractions to avoid increased damage to normal tissues. Provided this is ensured, the effect on late-responding tissues should be little altered by changes of time-structure, whilst additional repopulation in tumours and in acute-responding tissues is offset by keeping the total time unchanged. The strategy described involves a change in time-structure to compensate for a time effect (the gap), and does not require a "trade-off" of time and dose.

Of course, the strategy is only feasible in the case of gaps that are sufficiently short in relation to the treatment time remaining such that it is still possible to keep the total time constant. Large gaps, which cause the original treatment time to be exceeded before therapy resumes, cannot be completely allowed for in this way although the therapeutic disadvantage could be reduced. Greater importance consequently attaches to gaps occurring later rather than earlier in treatment, since the opportunity for post-gap adjustment of the time-structure will be less.

The feasibility of the strategy may also be limited by practical considerations. Where a gap involving many patients occurs as a result of machine breakdown, it may be impractical to institute post-gap acceleration for all such patients. Patients might then be selected for post-gap acceleration on the basis of potential doubling time of tumour type (Trott & Kummermehr, 1985).

Radiobiological processes other than repopulation

The consequences of gaps in treatment cannot be considered exclusively in terms of repopulation. Redistribution is also likely to be an important process, with gaps allowing increasing time for reassortment of surviving clonogenic cells in both normal tissues and tumours. It is possible that clonogenic cells in late-responding tissues reassort relatively slowly. Gaps would then be relatively disadvantageous to such tissues and accelerated fractionation relatively sparing. It is also conceivable that gaps might allow increased time for tumour reoxygenation. The generally poor therapeutic effects of treatment time prolongation (Thames & Hendry, 1987) do not suggest that this is likely to be an important factor. However, the possibility that post-gap acceleration might allow insufficient time for reoxygenation during this phase of treatment cannot yet be excluded. Accumulating evidence on the efficacy of regimes that are uniformly accelerated throughout should provide relevant evidence. Mitotic delay is not expected to be an important factor on the basis of *in vitro* evidence, but should it prove greater than expected, this would tend to favour the strategy of post-gap acceleration, which would preferentially stop repopulation in the tumour and acute-responding tissues, with little effect on non-repopulating, late-responding tissues. There seem to be no strong grounds for expecting post-gap acceleration to be therapeutically disadvantageous rather than otherwise.

Conclusions

Evidence exists that implies that unintended gaps leading to increased total time may be important in facilitating tumour repopulation. Compensatory strategies involving changes in total dose or dose per fraction are beset by problems. A strategy of post-gap acceleration of fractionation involves fewer radiobiological difficulties; this strategy is most clearly indicated for tumours likely to be capable of fast repopulation occurring in sites where dose limitation is imposed by tolerance of late-responding normal tissues.

References

AHERNE, W. & BUCK, P., 1971. The potential cell doubling time in neuroblastoma and nephroblastoma. *British Journal of Cancer, 25,* 691–696.

ELLIS, F., 1969. Dose, time and fractionation: a clinical hypothesis. *Clinical Radiology, 20,* 1–7.

DEEHAN, C. & O'DONOGHUE, J. A., 1988. Biological equivalence between fractionated radiotherapy treatments using the linear quadratic model. *British Journal of Radiology, 61,* 1187–1188.

FERTIL, B. & MALAISE, E. P., 1985. Intrinsic radiosensitivity of human cell lines is correlated with radioresponsiveness of human tumours. An analysis of 101 published survival curves. *International Journal of Radiation Oncology, Biology, Physics, 11,* 1699–1707.

FIELD, S. B., HORNSEY, S. & KUTSUTANI, Y., 1976. Effects of fractionated irradiation on mouse lung and a phenomenon of slow repair. *British Journal of Radiology, 49,* 700–707.

FOWLER, J. F., 1984. What next in fractionated radiotherapy? *British Journal of Cancer, 49,* Supplement vi, 285–300.

FOWLER, J. F., 1989. The linear quadratic model and progress in fractionated radiotherapy. *British Journal of Radiology, 62,* 679–694.

HALL, E. J., 1988. *Radiobiology for the Radiologist,* 3rd edn (J. B. Lippincott, Philadelphia).

KIRK, J., GRAY, W. M. & WATSON, E. R., 1971. Cumulative radiation effect. Part 1: Fractionated treatment regimes. *Clinical Radiology, 26,* 159–176.

MICHALOWSKI, A., 1981. Effects of radiation on normal tissues: hypothetical mechanisms of limitations of in situ assays of clonogenicity. *Radiation Environmental Biophysics, 19,* 157–172.

ORTON, C. G. & ELLIS, F., 1973. A simplification in the use of the NSD concept in practical radiotherapy. *British Journal of Radiology, 46,* 529–537.

STEEL, G. G., 1977. *Growth Kinetics of Tumours* (Clarendon Press, Oxford).

THAMES, H. D., PETERS, L. J., WITHERS, H. R. & FLETCHER, G. H., 1983. Accelerated fractionation versus hyperfractionation: rationales for several treatments per day. *International Journal of Radiation Oncology, Biology, Physics, 9,* 127–138.

THAMES, H. D. & HENDRY, J. H., 1987. *Fractionation in Radiotherapy* (Taylor & Francis, London).

TROTT, K. R. & KUMMERMEHR, J., 1985. What is known about tumour proliferation rates to choose between accelerated fractionation or hyperfractionation? *Radiotherapy and Oncology, 3,* 1–9.

TURESSON, I. & NOTTER, G., 1984. The influence of the overall treatment time in radiotherapy on the acute reaction: comparison of the effects of daily and once-a-week fractionation on human skin. *International Journal of Radiation Oncology, Biology, Physics, 10,* 593–598.

WHELDON, T. E. & AMIN, A. E., 1988. The linear-quadratic model. *British Journal of Radiology, 61,* 700–702.

WILLIAMS, M. V., DENEKAMP, J. & FOWLER, J. F., 1985. A review of α/β values for experimental tumours: implications for clinical studies of altered fractionation. *International Journal of Radiation Oncology, Biology, Physics, 11,* 87–96.

WITHERS, H. R., TAYLOR, J. M. G. & MACIEJEWSKI, B., 1988. The hazard of accelerated tumour clonogen repopulation during radiotherapy. *Acta Oncologica, 27,* 131–146.

1990, *The British Journal of Radiology*, *63*, 120–124

An assessment of the sensitivity of *in vivo* ^{31}P nuclear magnetic resonance spectroscopy as a means of detecting pH heterogeneity in tumours: a simulation study

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Abstract. The presence of hypoxia and low pH in tumours is known to influence several treatment modalities including radiotherapy, chemotherapy and hyperthermia. Hypoxic and acidic regions have been demonstrated in tumours using pH and pO_2 microelectrodes. The technique has shown marked heterogeneity within individual tumours. A non-invasive measure of intracellular pH is provided by ^{31}P nuclear magnetic resonance (NMR) spectroscopy from determination of the chemical shift of inorganic phosphate, and is being increasingly applied to the study of human tumours *in vivo*. Based upon the assumption that hypoxic cells are also acidic, we have assessed the ability of a whole-body NMR spectrometer to detect acidic subpopulations within a tumour using simulated tumour spectra. In these simulations the size of the acidic subpopulation, assigned pH values from 5.0 to 7.0, was varied between 5% and 50% of the neutral "control" population. Gaussian noise was added to the simulated spectra giving signal-to-noise ratios for the neutral control inorganic phosphate peak of 3, 5 and 7, which are typical of values encountered in human tumour measurements. From the results of the simulations it seems unlikely that human hypoxic, and presumably acidic, cell fractions, typically 1–15%, will be detected by this method in the presence of signal-to-noise levels characteristic of current equipment. Therefore, whole-body *in vivo* ^{31}P NMR spectroscopy may fail to identify significant pH heterogeneity within human tumours. Improvements in signal-to-noise and line separation owing to improvements in technique and higher field strength instruments may improve sensitivity to heterogeneous populations.

The pH of tumours is known to influence several treatment techniques either directly or indirectly through inadequate tissue perfusion, resulting in impaired delivery of drugs or oxygen. The degree of tissue oxygenation may be inferred from tissue pH if it is assumed that cells in a hypoxic environment use predominantly anaerobic glycolysis rather than oxidative phosphorylation, resulting in the production of excess lactic acid. *In vivo* ^{31}P nuclear magnetic resonance (NMR) spectroscopy is a non-invasive technique which can be used to measure intracellular pH (pH_i) *in vivo* and has been applied to the study of both animal and human tumours. The technique may have considerable potential for monitoring the effects of treatment on tumour metabolism (Semmler et al, 1988; Ng et al, 1989; Glaholm et al, 1989).

In solid tumours, the cellular microstructure contains areas close to the capillaries where cells are well oxygenated and necrotic areas distant from the capillaries. Hypoxic, yet viable cells, some of which may have clonogenic potential, exist at intermediate distances (Thomlinson & Gray, 1955). Cellular hypoxia is an established cause of radioresistance to low linear energy transfer (LET) ionizing radiation as produced by clinical linear accelerators or ^{60}Co γ-ray units. The existence of such hypoxic cells should result in lactic acid production with an associated fall in tissue pH. A low extracellular pH (pH_e) has been shown to produce radioresistance in human glial cells and Chinese hamster ovary (CHO) cell cultures (Rottinger & Mordanca, 1982). Furthermore, the degree of fixation of potentially lethal radiation damage is reduced in CHO cells cultured in an acidic environment (Freeman & Sierra, 1984). Hypoxic and acidic environmental conditions have been exploited in the design of hypoxic cell sensitizers (Fowler, 1985). In contrast to radiotherapy, the cytotoxic effect of hyperthermia is enhanced in an acidic environment (Overgaard, 1975). Hyperthermia may, therefore, complement low LET ionizing radiation by eradicating hypoxic and presumably acidic, radioresistant, clonogenic cells.

Insufficient oxygenation is often indicative of an inadequate blood supply, which would in turn result in impaired cytotoxic drug delivery. More specifically, the activities of several commonly used cytotoxic agents are modified by environmental pH. Adriamycin has been shown to be less effective at low pH in Chinese hamster cells in culture, an effect which was more pronounced in well oxygenated cells (Born & Eicholtz-Wirth, 1981). In contrast, an optimum pH of 6.8 has been demonstrated for the cytotoxicity of 5-fluorouracil in cultured human mesothelioma cells (Nissen & Tanneberger, 1981), and the cellular uptake of chlorambucil is enhanced *in vitro* at low pH in transformed Chinese hamster ovary cells (Mikkelsen & Wallach, 1982).

The presence of even a small subset of clonogenic cells at low pH may determine the success or failure of these therapeutic techniques. An *in vivo* measurement of intracellular pH (pH_i) is provided by ^{31}P NMR spectroscopy, determined by the frequency shift of the inorganic phosphate (P_i) peak relative to the phosphocreatine peak (Moon & Richards, 1973). Splitting or broadening of the peak may indicate the presence of two or more populations of cells at differing pH, *i.e.* heterogeneity. Human hypoxic fractions are typically 1–15% (Moulder & Rockwell, 1984; Urtasun et al, 1986). The ability to detect small pH subpopulations typical of human tumours *in vivo* may, however, be limited by the current sensitivity of whole-body NMR systems.

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This study investigates the probability of detecting a low pH subpopulation in human tumours using a 1.5 Tesla whole-body NMR system, by simulating a series of spectra in the presence of background noise.

Materials and methods

Modelling hypoxic subpopulations

In order to investigate the sensitivity of ^{31}P NMR spectroscopy as a means of detecting the presence of small subpopulations of hypoxic and presumably acidic cell fractions in human tumours, a range of spectra were simulated. The spectral characteristics were chosen to be typical of those we commonly measure *in vivo* with a resolution of 0.2 ppm (parts per million). The control P_i population was assigned a pH of 7.0, and the pH of the P_i subpopulation was varied between 5.0 and 7.0 by increments of 0.25, while its proportion relative to the size of the control population was varied between 5% and 50%, in steps of 5%.

Simulated spectra included five peaks, typical of human tumours, in the range of 0.0 to 10.0 ppm superimposed on the broad phospholipid baseline. These corresponded to phosphocreatine (PCr), phosphomonoesters (PME), phosphodiesters (PDE) and two P_i peaks representing the control population and the acidic subpopulation. However, the nucleotide triphosphate peaks were not included because their resonant frequency is far removed from the P_i peak and therefore would not obscure P_i peak detection. Typical signal-to-noise ratios (SNRs) were measured on a number of clinical spectra yielding values between 3 and 7 for the P_i peak as defined by Gadian (1982):

$$\text{SNR} = \frac{2.5x\text{P}_{i(\text{control})}\ \text{signal}}{\text{peak-to-peak noise}}$$

These spectra were obtained from large breast tumours using a 5 cm diameter surface coil and Conformal ISIS localization (Sharp & Leach, 1989). Acquisition times were typically 40 min and the resultant localized free induction decay (FID) was multiplied by an exponential filter with a 20 ms decay constant. Gaussian noise was therefore added to the simulations to give signal to noise ratios for the P_i peak of 3, 5 and 7. It was assumed that the noise was random, time-independent and unaffected by Fourier transformation. Simulated spectra were processed using the same technique of exponential smoothing as employed in *in vivo* tumour measurements.

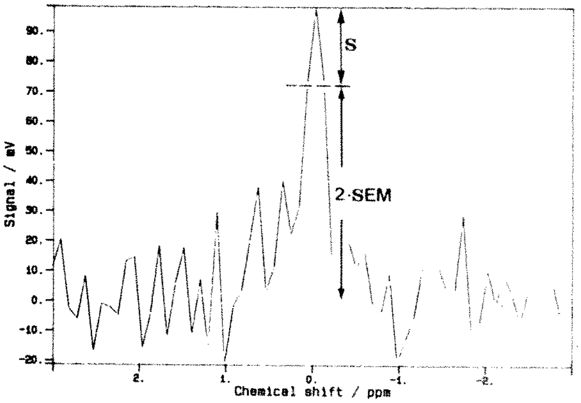


Figure 1. Graphical representation of the peak significance assessment criterion. Peak height must be greater than twice the standard error of the mean (SEM) of the noise distribution for the peak to be significant at the 95% confidence level.

Assessment of peak significance

In order to define criteria for peak significance, the noise characteristics must first be determined. A region was selected in the real, phased spectrum where no metabolites were present and where the signal was not attenuated by the analog filter. A simple baseline correction was adopted by performing a trapezium subtraction based on the minimum points at each side of the P_i peak. This ensured that the baseline was flat in order to avoid overestimation of noise. The mean and standard error of the amplitude of the noise were estimated assuming a Gaussian noise distribution. The presence of correlation between neighbouring points, introduced by the exponential smoothing function, was investigated and its effect on the noise characteristics was taken into account in the calculations. The peak detection criterion was defined by

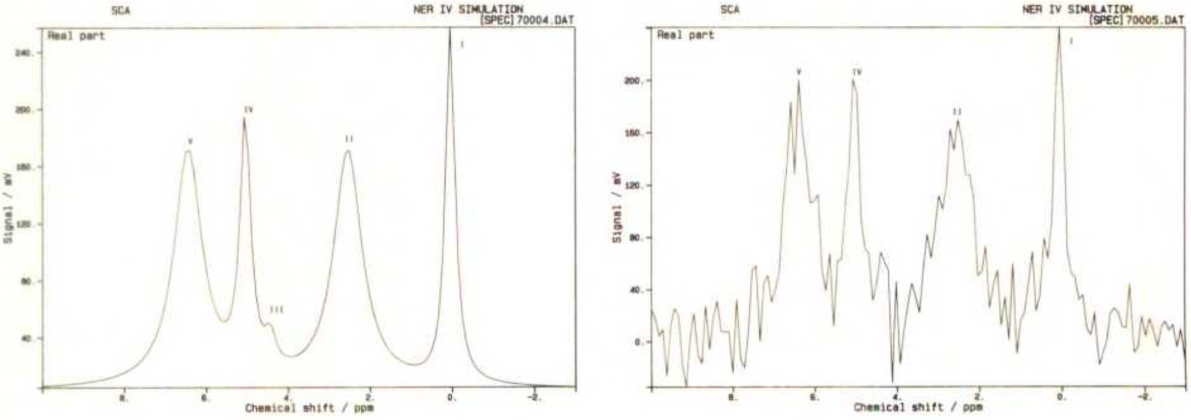
$$(\text{Peak Height}) > 2 \times \text{SEM}$$

where SEM is the standard error of the mean of the noise (Fig. 1). Peaks satisfying this criteria will be significant at the 95% confidence level (Avraamidou et al, 1988; Madden et al, 1990).

Results

A typical spectrum before and after the addition of Gaussian noise is shown in Fig. 2. The control population was assigned a pH of 7.0 (peak IV), while in this example the subpopulation has been taken to be 10% of the control, with an assigned pH of 6.7 (peak III). The subpopulation is visible in Fig. 2(a); however, following the addition of Gaussian noise, the peak becomes insignificant to 95% confidence.

In order to investigate the threshold sensitivity of the system, a series of spectra were simulated, with acidic fractions ranging from 5% to 50% at different pH values, and also for the SNR of 3, 5 and 7 as determined using the control P_i peak. The results of the significance assessment are shown graphically in Fig. 3. Sharp tran-



(a) (b)

Figure 2. Spectral simulations (a) before and (b) after addition of Gaussian noise. The peak assignments are I—phosphocreatine; II—phosphodiesters (PDE); III—P_i subpopulation; IV—control P_i and V—phosphomonoesters (PME). Note that the P_i subpopulation (III) becomes insignificant following addition of noise.

sitions between the different percentage fractions required for detection result from the fact that the percentage fraction of the acidic subpopulation present was increased in steps of 5% rather than as a continuum. At a pH of 6.5, the subpopulation is only detected when it comprises more than 15% of the control population for the optimum SNR value of 7, while for a pH of 6.25 or 6.0, only when it is larger than 20% of the control. For an SNR of 5, the subpopulation is only detected for a fraction of 35% or greater at a pH of 6.25, while a fraction of at least 40% is required at a pH of 6.5 and at least 50% for a pH of 6.0. In the worst case investigated (SNR = 3), the minimum fraction required for detection was 40% at a pH of 6.5, while fractions of 50% or greater were required for a pH of 6.0 or 6.25.

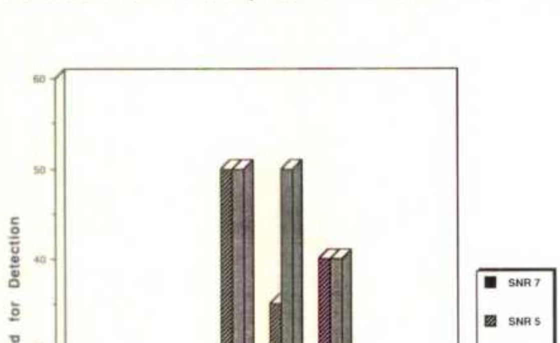


Figure 3. Graphical representation of the percentage fraction of the cell subpopulation required for detection. Different SNRs were tested, but even for the best case of SNR simulated (7), the minimum fraction required was 15%. Since human hypoxic, and presumably acidic, fractions are typically 1–15%, the majority of these would not be detected.

For subpopulations assigned pH values greater than 6.5, the peak merges with the control inorganic phosphate (P_i), and for a pH less than 6.0 the subpopulation is masked by the broad phosphodiester (PDE) peak. These problems are compounded by difficulties in defining a baseline from which the peak height can be measured reliably. Cell subpopulations having a pH of less than 6.0 or greater than 6.5 would, therefore, not be detected within the SNR range simulated.

In the intermediate pH region, 6.0 to 6.5, detection of small acidic fractions is primarily dependent on the SNR (Fig. 3). Even with the optimal SNR of 7, a minimum subpopulation of 15% of the control is required for peak detection. Since human hypoxic fractions are typically in the range of 1–15%, even with good SNRs the majority of hypoxic, and presumably acidic, cell subpopulations would not be detected.

Discussion

The majority of *in vivo* tumour pH measurements in animal models have been obtained using microelectrodes. Tissue damage is an inevitable consequence of this technique, and therefore the measured pH is likely to be a combination of both extracellular (pH_e) and intracellular (pH_i) pH. However, such studies have proven valuable for demonstrating heterogeneity in intact tumour systems. Vaupel et al (1981) measured

pH_e and pO_2 in the C3H mouse mammary tumour using 1 μm diameter microelectrodes, and found pH and pO_2 heterogeneity within different micro-areas of the same tumour. Low pH values of 5.8 to 6.3 were recorded in large ulcerated tumours, whilst high local pH readings were obtained in necrotic areas. Heterogeneity of pH has also been observed in other animal models using this technique (Jähde et al, 1982).

It is important to discriminate between pH_e and pH_i, because their interrelationship may depend upon other extracellular conditions. In particular, it has been shown that Ehrlich ascites tumour cells are able to maintain their intracellular pH in an acidic external environment when well oxygenated, but not when rendered anoxic (Gillies et al, 1982). Since hypoxic and acidic conditions are presumed to co-exist in intact human tumours, it seems probable that cells in such an environment might develop a low intracellular pH.

Both ^{31}P NMR spectroscopy and weak acid partitioning (5,5-dimethyloxazolidine-2,4-dione (DMO)) are non-invasive techniques which can be used to measure pH_i in tissues *in vivo*. *In vitro* measurements of pH_i in CHO fibroblasts have shown good correlation between the two methods (González-Méndez et al, 1988). The DMO technique measures an average pH_i within a volume of interest and has demonstrated normal or high pH_i values in human brain tumours *in vivo* (Rottenberg et al, 1984). With ^{31}P NMR spectroscopy, the pH_i is measured from the frequency shift of the P_i peak, and splitting or broadening of this peak may indicate tissue pH_i heterogeneity. Broadened P_i peaks, suggesting pH_i heterogeneity, have been demonstrated in unlocalized spectra from the brains of unanaesthetized mice (Hitzig et al, 1985) and also in human brain tumours *in vivo* (Segebarth et al, 1987). Ng et al (1989) have recently reported overlapping P_i peaks in the tumour of a patient undergoing combined radiotherapy and chemotherapy treatment, suggesting pH heterogeneity. However, Oberhaensli et al (1986) examined 15 human tumours of different histologies and found narrow P_i peaks, which would suggest pH homogeneity. Interpretation of apparent heterogeneity in P_i peaks depends on the nature and accuracy of the localization techniques employed, as inadequate localization can result in sampling of adjacent normal tissues.

The sensitivity of an NMR spectroscopy system in detecting small subpopulations of differing pH_i must be established before any conclusions can be drawn regarding tumour pH heterogeneity. We have simulated the performance of an *in vivo* whole-body NMR spectrometer operating at 1.5 Tesla to determine its ability to distinguish two hypothetical pH subpopulations, given a range of pH subpopulation fractions and SNRs typical of the system. The low SNRs and the ill-defined baseline on which the peaks are superimposed severely limit the sensitivity of the technique.

In the intermediate pH region of 6.0 to 6.5, peak detection is mainly dependent upon the SNR. However, a subpopulation with a pH_i greater than 6.5 or less than 6.0 would tend to be obscured by the adjacent PDE and principle P_i peaks respectively. Therefore, the sensitivity of the system in detecting small subpopulations may be increased with an improvement in SNR. However, even in our example of the highest SNR typically observed in *in vivo* breast tumour spectra, a minimum subpopulation size of 15% would be required for detection. It must also be borne in mind that the simulation has assessed a "best case" situation with relatively good line width and in the absence of the very broad phospholipid baseline, which may result in peak overlap between the PME, PDE and P_i peaks as well as in further peak shape distortions *in vivo*. These effects would further reduce the sensitivity.

Conclusions

With the current sensitivity of whole body *in vivo* spectrometers, a subpopulation of differing pH would be detected only if it comprised at least 15% of the main pH population. The sensitivity of the measurement is determined by the level of noise, metabolic activity, tissue type, surface coil and the proximity of the subpopulation P_i peak to adjacent peaks in the spectrum. Therefore, detection would be optimal when the P_i peak representing a pH subpopulation is equidistant from the adjacent P_i and PDE peaks.

Human hypoxic fractions are typically in the region of 1–15%. This apparently small proportion of cells may nevertheless provide a significant pool of treatment resistant clonogenic cells. Based upon the assumption that this cellular fraction is also acidic, similar whole-body systems would be unlikely to detect such cells. It is, therefore, conceivable that significant subpopulations of hypoxic, acidic cells may exist in human tumours, which appear to be homogeneous and neutral, or even alkaline when examined by *in vivo* ^{31}P NMR spectroscopy. Greater sensitivity may result from improvements in the SNR of whole-body systems through improvements in technique, improved coil sensitivity, increased magnetic field strength and the use of proton decoupled spectra.

References

AVRAAMIDOU, A., LEACH, M. O., SHARP, J. C. & EASTON, D., 1988. Quantitative analysis of the accuracy of pH measurements. In *Proceedings of the 7th Annual Meeting of the Society of Magnetic Resonance in Medicine, Book of Abstracts*, Vol. 2 (Society of Magnetic Resonance in Medicine, San Francisco, USA), p. 819.

BORN, P. & EICHOLTZ-WIRTH, H., 1981. Effect of different physiological conditions on the action of adriamycin on Chinese hamster cells '*in vitro*'. *British Journal of Cancer*, *44*, 241–246.

FOWLER, J. F., 1985. Chemical modifiers of radiosensitivity—theory and reality: a review. *International Journal of Radiation Oncology, Biology, Physics*, *11*, 665–674.

FREEMAN, M. L. & SIERRA, E., 1984. An acidic extracellular environment reduces the fixation of radiation damage. *Radiation Research*, *97*, 154–161.

GADIAN, D. G., 1982. *Nuclear Magnetic Resonance and its Application to Living Systems* (Clarendon Press, Oxford), pp. 8–10.

Gillies, R. J., Ogino, T., Shulman, R. G. & Ward, P. C., 1982. ^{31}P NMR evidence for the regulation of intracellular pH by Ehrlich ascites tumor cells. *The Journal of Cell Biology, 95*, 24–28.

Glaholm, J., Leach, M. O., Collins, D., Mansi, J., Sharp, J. C., Madden, A., Smith, I. E. & McCready, V. R., 1989. *In vivo* ^{31}P magnetic resonance spectroscopy for monitoring the treatment response of human breast carcinoma. *The Lancet, i*, 1326–1327.

González-Méndez, R., Hahn, G. M., Wade-Jadetzky, N. G. & Jadetzky, O. 1988. Comparison of intracellular pH measurements by ^{31}P NMR and weak acid partitioning in Chinese hamster ovary fibroblasts. *Magnetic Resonance in Medicine, 6*, 373–380.

Hitzig, B. M., McFarland, E., Johnson, D. C., Koutcher, J. A., Elmden, K., Neuringer, L. & Kazemi, H., 1985. Brain cell pH and high energy phosphates during hypercarnia and hypoxia in unanaesthetised mice. *Proceedings of IVth Annual Meeting of the Society of MR in Medicine*, Vol. I (Society of Magnetic Resonance in Medicine, London), pp. 479–480.

Jähde, E., Rajewsky, M. F. & Baumgartl, H., 1982. pH distributions in transplanted neural tumors and normal tissues of BDIX rats as measured with pH microelectrodes. *Cancer Research, 42*, 1498–1504.

Madden, A., Leach, M. O., Sharp, J. C., Collins, D. & Easton, D., 1990. A quantitative analysis of the accuracy of *in vivo* pH measurements with ^{31}P NMR spectroscopy. *NMR in Biomedicine* (submitted for publication).

Mikkelsen, R. B. & Wallach, D. F. H., 1982. Transmembrane ion gradients and thermochemotherapy. In *Biomedical Thermology*. Ed. by M. Gantherie & E. Albert (Alan R. Liss, New York), pp. 103–107.

Moon, R. B. & Richards, J. H., 1973). Determination of intracellular pH by ^{31}P magnetic resonance. *The Journal of Biological Chemistry, 242*, 7276–7278.

Moulder, J. E. & Rockwell, S., 1984. Hypoxic fractions of solid tumors: experimental techniques, methods of analysis, and a survey of existing data. *International Journal of Radiation Oncology, Biology and Physics, 10(5)*, 695–712.

Ng, T. C., Majors, A. W., Vijayakumar, S., Baldwin, N. J., Thomas, F. J., Koumoundouros, I., Taylor, M. E., Grundfest, S. F., Meaney, T. F., Tubbs, R. R. & Shin, K. H., 1989. Human neoplasm pH and response to radiation therapy: ^{31}P MR spectroscopy studies in situ. *Radiology, 170*, 875–878.

Nissen, E. & Tanneberger, S. T., 1981. Influence of pH and serum on the effectivity of antineoplastic agents '*in vitro*'. In *Archives Geschwulstforsch, 51*, 152–156.

Oberhaensli, R. D., Hilton-Jones, D., Bore, P. J., Hands, L. J., Rampling, R. P. & Radda, G. K., 1986. Biochemical investigation of human tumours '*in vivo*' with phosphorus-31 magnetic resonance spectroscopy. *The Lancet, ii*, 8–11.

Overgaard, J., 1975. Effect of pH on response to hyperthermia. In *Proceedings of the Symposium on Cancer Therapy with Hyperthermia and Radiation* (Taylor and Francis, Washington, USA), p. 43.

Rottenberg, D. A., Ginos, J. Z., Kearfott, K. J., Junck, L., Dhawan, V. & Jarden, J. O., 1984. '*In vivo*' measurement of brain tumor pH using ^{11}C DMO and positron emission tomography. *Annals of Neurology, 17*, 70–79.

Röttinger, E. M. & Mordanca, M., 1982. Radioresistance secondary to low pH in human glial cells and Chinese hamster ovary cells. *International Journal of Radiation Oncology, Biology, Physics, 8*, 1309–1314.

Segebarth, C. M., Baleriaux, D. F., Arnold, D. L., Luyten, P. R. & den Hollander, J. A., 1987. MR image-guided ^{31}P MR spectroscopy in the evaluation of brain tumor treatment. *Radiology, 165*, 215–219.

Semmler, W., Gademann, G., Bachert-Baumann, P., Zabel, H. J. & Lorenz, W. J., 1988. Monitoring human tumor response to therapy by means of ^{31}P MR spectroscopy. *Radiology, 166*, 533–539.

Sharp, J. C. & Leach, M. O., 1989. Conformal NMR spectroscopy: accurate localisation to non-cuboidal volumes with optimum SNR. *Magnetic Resonance in Medicine*, Vol. II (Society of Magnetic Resonance in Medicine, London), pp. 376–388.

Thomlinson, R. H. & Gray, L. H., 1955. The histological structure of some human lung cancers and the possible implications for radiotherapy. *British Journal of Cancer, 9*, 539–549.

Urtasun, R. C., Chapman, J. D., Raleigh, J. A., Franko, A. J. & Koch, C. J., 1986. Binding of 3H-Misonidazole to solid human tumors as a measure of tumor hypoxia. *International Journal of Radiation Oncology, Biology, Physics, 12*, 1263–1267.

Vaupel, P. W., Frinak, S. & Bicher, H. I., 1981. Heterogeneous oxygen partial pressure and pH distribution in C3H mouse mammary adenocarcinoma. *Cancer Research, 41*, 2008–2013.

1990, *The British Journal of Radiology*, *63*, 125–127

Dosimetric intercomparison in the British Institute of Radiology fractionation study of 3F/week versus 5F/week in radiotherapy of laryngo-pharynx cancer

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Abstract. A dose intercomparison was carried out by the National Physical Laboratory between the seven radiotherapy centres which contributed the largest number of patients to the British Institute of Radiology fractionation study of three fractions per week versus five fractions per week in clinical cancer treatment. Six of the centres showed remarkable agreement within the acceptable limits of error of the measurements. In one centre there appeared to be a physical dose discrepancy of 2.8% which was materially less than could be detected clinically.

As part of the long-term clinical trial on dose fractionation organized by the Fractionation Working Party of the British Institute of Radiology (BIR Working Party, 1982), a dose intercomparison between the seven participating radiotherapy centres which contributed the largest number of patients was carried out by the National Physical Laboratory (NPL).

Materials and methods

The intercomparison took the form of in-phantom irradiations of Fricke dosimeters to a series of specified doses during two periods in 1978–1979. Dosimeters and phantoms were supplied by the Chemical Dosimetry Group in the NPL, who also carried out the measurements on the irradiated dosimeters. The physicist at each centre organized a normal treatment of larynx and pharynx cancer, applied as a single field with either cobalt 60 or higher energy X rays, asking the radiographers and treatment planners to set up the irradiation as they would a patient. This was followed by an immediate in-phantom measurement of dose-rate using a thimble ionization chamber, then repeat measurements after the phantom had been removed and repositioned by the radiographers.

Special emphasis was put on the necessity not to alter the assessment of dose based on the individual centre's normal procedure and used for the first dose measurement, as the interest in the dose intercomparison lay in the dose actually received in typical clinical treatments and was not intended to be an exercise in checking the calibration of the ionization chamber. Similarly, care was taken to follow exactly what the treatment planners specified as the irradiation conditions for a normal set-up for a carcinoma of larynx radical treatment field size. The successive measurements were performed after the radiographers repositioned the phantom as they would have done a patient in a fractionated course of irradiation.

The Fricke dosimeters and water phantom were supplied by NPL and were of the type normally used for the NPL Fricke Dosimeter Service. The dosimeter solution was sealed in pharmaceutical glass ampoules of nominal volume 2 cm^3. The phantom was a cubic plastic tank (sides 250 mm × 250 mm). An inner Perspex plate with a vertical hole accepted the Fricke ampoule, or an ionization chamber in an adaptor sleeve thus providing simple substitution at a fixed depth. For the present intercomparison, a depth of 50 mm was chosen. The treatment planners were asked to assume that this included a total thickness of 14 mm Perspex of density 1.2 g/cm^3.

First dose intercomparison, June, 1978

The doses specified for the first run were 20, 30 and 40 Gy. Ten dosimeters were supplied allowing a duplicate at each level and four controls. Two centres used 4 MV X rays, the remainder cobalt 60. After irradiations were complete, the Fricke dosimeters were returned to the NPL for measurement. Unfortunately, it became apparent at this point that some dosimeters from the batch prepared for this work had developed abnormally high readings. The incidence of abnormal dosimeters was about one in ten, observed in the controls. The cause of this abnormality was traced and steps taken to prevent its recurrence.

Although four of the centres showed 95% confidence limits as narrow as ±0.8–1.2%, the other three showed ±3.7% and it was concluded that these were affected by the abnormal readings. There was also a spread of 6.6% between the readings of the four, and this discrepancy made it necessary to repeat the excercise. In response to many requests, one change was made: a deletion of the highest dose of 40 Gy and the addition of a dose of 10 Gy. This reduced total exposure times by 50% and was of particular benefit to the two centres using accelerators.

Second dose intercomparison, February, 1979

The whole exercise, detailed above under the first dose intercomparison, was repeated in February, 1979 with only the following amendments.

A clinical larynx set-up, in one of the centres for example, consisted of the patient lying on the treatment couch with the head and shoulders located in an individually constructed treatment jig which then had a Perspex anterior neck moulding clipped on to it thus ensuring exact, three-dimensional reproducibility for each irradiation session. The anterior moulding, with a small portion of Perspex cut away over the treatment area in order to cut down the skin reaction, carried a framework into which the applicator that was attached to the treatment machine could be guided accurately. The applicator carried a guide channel into which an individually constructed compensator plate was slotted to avoid both hot spots from air gaps and low-dose regions due to oblique tissue absorption. The correct alignment of the treatment portals on the jig was confirmed by a localizing radiograph before the treatment started. For the purposes of this dose intercomparison, a treatment applicator of the field size used for a clinical larynx treatment was aligned with the NPL tank.

Results

Because of the technical problems encountered in the first dose intercomparison in June, 1978, the detailed data from this excercise are not included in this report. The results obtained in the second dose intercomparison in February, 1979 are shown in Table I. The ratio of measured to calculated dose has been normalized about the overall mean. The data then represent the spread of underdosing or overdosing between the seven centres, *e.g.* 1.01 represents a 1% overdose compared with the overall mean of all centres.

Of the two missing observations shown in Table I, one ampoule was broken in transit, the other gave a result 50% higher than that estimated by the centre. The value of 1.036 in column G can be classed as an outlier, being more than six standard deviations away from the mean. The mean and standard deviation of set G excludes this value. In the case of centre A, the checks which were made using an ionization chamber immediately after irradiation of the Fricke dosimeters indicated a dose rate 1.5% lower than that calculated. This was later confirmed by a measurement using an NPL calibrated secondary standard chamber, and contributory causes were shown to be (a) cobalt 60 decay since the last correction (corrections were applied every two months) amounting to about 0.7% and (b) the effect of the Perspex in the beam on the depth factor—about 0.5%. The treatment planners had, quite rightly, in treating the phantom as a normal patient, ignored these small corrections as set out specifically under the "Materials and methods" section. A further small difference of 0.5% was found to exist between centre A and the NPL in that their choice of C_λ factor, a chamber correction factor, differed: the NPL used 0.945, whereas centre A used 0.95. The values shown in column A of Table I represent, therefore, the original values that have been multiplied by a correction factor of 1.02 to take account of these corrections. The resulting mean ratio was then 0.972 as shown. It was found at centre F that an incorrect barometer reading contributed a correction of 0.8% in the centre's ionization monitor. This, together with a wedge factor correction of 1.3% under the phantom irradiation conditions, meant that the original values in column F had to be divided by 1.0216. The resulting mean ratio was then 1.008 as shown.

The data in Table I were derived by first calculating for each observation the ratio R_c from the absorbed dose estimated by the centre and the absorbed dose stated by the NPL. The overall mean of all ratios $\bar{R}_c$ was then calculated. The normalized relative mean doses in the table were then calculated as the ratio $R_c/\bar{R}_c$. The standard deviations in Table I are calculated from the results of each centre. A rather more pessimistic and realistic view of the uncertainties can be taken by calculating 95% confidence limits for the mean of each centre based on the overall standard deviation and the number of observations in each set (Table II). The second column in Table II is derived by subtracting unity from the mean dose for each centre and expressing the result as a percentage. The third column is derived by calculating for each centre the standard error of the mean S

Table I. Normalized relative measured doses using Fricke dosimeters at the seven centres (A–G) at various dose levels

Nominal dose (Gy)	Centres						
	A	B	C	D	E	F	G
10	0.971	1.009	1.006	1.010	1.008	0.998	1.006
10	0.965	1.010	Missing	1.011	1.009	0.990	[1.036][a]
20	0.974	1.012	0.985	1.002	0.997	1.001	1.001
20	0.973	1.008	0.992	1.008	0.998	1.026	Missing
30	0.976	1.007	0.990	1.002	0.999	1.011	1.001
30	0.974	1.008	0.991	0.997	0.997	1.024	1.003
Mean	0.972	1.009	0.993	1.005	1.001	1.008	1.003
Standard Deviation	0.004	0.002	0.008	0.006	0.006	0.015	0.002

[a] Outlying value.

Table II. Mean measured dose for each centre expressed as a deviation from the norm and 95% confidence limits derived from the spread of dose measurements

Centre	Mean deviation from norm (%)	95% limit (± %)
A	−2.8	0.8
B	+0.9	0.8
C	−0.7	0.9
D	+0.5	0.8
E	+0.1	0.8
F	+0.8	0.8
G	+0.3	1.2

of the ratio $R_c/\bar{R}_c$ where S = overall sd/$\sqrt{n}$ and multiplying by a t factor at $p = 95\%$, appropriate to the number of degrees of freedom. For example, the overall sd is 0.0074, and for centre A with six observations, $S = 0.0074/\sqrt{6} = 0.003$. For six observations, the degree of freedom is 5 and the t value at $p = 95\%$ is 2.57 (from standard tables). The value of S for the centre is thus 0.0077, rounded to 0.8%.

A visual examination of the results presented in Table II shows that all except one centre are within ±1% of the mean of all centres.

Discussion

A comparison of the deviation from the mean for centre A with its confidence limit shows clearly that it is significantly different from the mean of all centres. The results of this centre confirm the findings in the first run in June, 1978 which showed a similar discrepancy. Because of the discrepancies, all the data from centre A were submitted to the NPL for checking of the workings and no errors were identified.

The 2.8% dose discrepancy noted in centre A has to be considered against the background of the biological effect of such a change in radiation dose. Because of the material variations in the radiation response of individual patient's tissues compared with those of other patients, in addition to the variations in radiation response between different anatomical structures in the same patient, it is commonly accepted that it is not possible to identify clinically changes in physical radiation dose that are smaller than 5% when standard fractionation regimes are used. It is not surprising, therefore, that no differences have been noted in the results reported from the various participating radiotherapy centres (BIR Working Party, 1990).

At centre F an intial deviation of 3% from the NPL values was found to be a result of an incorrect barometer reading (0.8%) and a wedge factor error of 1.3%, under the test conditions, giving a 1.02% correction. The particular test conditions at centre F, a single-wedged field entering the phantom at an angle of 35°, coupled with a very small field size of 5 cm × 5 cm, appears to represent the most stringent test conditions amongst the centres.

Although not essential to the intercomparison, it is of interest to point out that the overall mean ratio of measured dose at the NPL to calculated dose at the centres was 1.008, taking into account all the correction factors referred to in this paper. In other words, the absorbed dose to the Fricke ampoules as measured by the NPL was 1.008 times greater than the absorbed dose calculated by the centres on average. This is extremely close to unity, bearing in mind the fact that the conditions set for this intercomparison between centres were quite inappropriate for a calibration excercise.

Conclusions

Excluding centre A, the six other centres show remarkable agreement both with the NPL and with each other within ±1%, with an uncertainty of ±1.4% at the 95% confidence levels, *i.e.* they agree within acceptable limits of error of the measurements.

The difference in measured doses between centre A and the mean of the other six, regarding the Fricke dosimeters and phantoms as a transfer standard linking the ionization chambers in the centres, appears to be of the order of 3.2%. Despite strenuous efforts to identify the cause for this discrepancy, none has been found. No differences were obvious in the clinical results between centres.

References

BIR Working Party, 1982. Seventh Interim Progress Report of the British Institute of Radiology fractionation study of 3F/week versus 5F/week in radiotherapy of the laryngo-pharynx. *British Journal of Radiology, 55*, 505–510.

—— 1990. Final Report of the general clinical results of the British Institute of Radiology fractionation study of 3F/week versus 5F/week in radiotherapy of carcinoma of the laryngo-pharynx. *British Journal of Radiology*, in press.

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Technical note

Further comparisons of films, screens and cassettes for mammography

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In two previous papers (Kirkpatrick & Law, 1987, Law & Kirkpatrick, 1989), films and screens for mammography have been compared, primarily for image quality and secondarily for dose. The rate at which new products become commercially available makes identification of the better films and screens a never-ending task, although the combination found to be still the best in 1987 had been available since before 1980. At the time of the work for the 1989 paper (late 1987) certain newer products did offer some improvement over previous ones, but further products were known to be imminent. That series of comparisons could not be continued because the processor was changed making it impossible to maintain complete comparability of test conditions.

This paper reports on new films and screens, using essentially the same experimental technique as before, but on a new processor and a new X-ray set. Certain of the better films and screens from the previous paper were included to form a base line against which to compare newer products. Only a direct comparison under a single set of experimental conditions can be considered valid.

Experimental technique

All films were obtained on a single X-ray set and a single processor. These were a CGR 600t mammographic X-ray set installed as the assessment unit in the Edinburgh Breast Screening Centre, and a Dupont T5A processor using Kodak chemistry. The X-ray set has Molybdenum target and filtration and broad and fine foci. All films were contact films obtained at a nominal 25 kV using the broad focus, nominal size 0.3 mm, at 60 cm focus–film distance (FFD). The actual kV was checked with a calibrated digital kV meter (Law et al, 1989) and estimated to be about 24.5 kV. The measured size of the focal spot, in the region where the test object was placed, was estimated by slit, pin-hole and star tests to be about 0.35mm × 0.5 mm. The processor was run at 35°C and 2.5 min for purposes of this work.

In other respects the technique was unchanged from the previous work already cited. A "Barts" test object or phantom was used (White & Tucker, 1980) and sets of six films each were obtained for every film–screen combination considered. Manual exposure control was used throughout, the mAs being selected to give approximately unit density under clear parts of the phantom. The mAs required for density 1.0 was then calculated to enable dose comparisons to be made. Films were scored by both authors independently and combined as previously described (Kirkpatrick & Law, 1987).

Wherever possible, films and screens were exposed in heat-sealed black plastic envelopes rather than cassettes in order to produce optimal, and strictly comparable, conditions. Results for selected films and screens were obtained in cassettes for comparison.

The MinR film and screen combination was retained as a standard in this work, and results were obtained using it on almost every day on which tests were done, extending to a period of over 4 months. This allowed the consistency of X-ray set performance, processing and film scoring to be monitored. In selected cases where the results seemed interesting, a limited number of repeat sets of films were obtained from other film–screen combinations in order to reduce experimental uncertainties.

Results

MinR films and screens

Nine sets of films were obtained. The mean image score was 55.8 ± 0.3 (standard error on the mean, 68% confidence interval) with a standard deviation for a single set of 0.9.

Other Kodak products

Two new types of screen were supplied and one new type of film. The new screens were MinR medium and MinR fast. The former is a single screen while the latter is a pair of front and back screens, the back screen being of the MinR medium type.

Initially, three cassettes were supplied fitted with each of the newer kinds of screen. These cassettes appeared indistinguishable from previous Kodak MinR cassettes supplied with ordinary MinR screens, and X-ray attenuation in the front face also appeared the same. However, there did appear to be a greater thickness of foam behind the back screens which could have led to better film–screen contact. Later, medium and fast screens were supplied loose for use in envelopes.

The new film, T-matM "revised", is of double emulsion type, intended principally for use with MinR fast

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Table I. Image scores and relative doses for Kodak products

	Film	Screen		
		MinR	MinR medium	MinR fast
Image scores	MinR	55.8±0.3 (9)	54.3±0.8[a] 53.0±0.6	54.6±0.4 (2)[a]
	OMI	54.8±0.4 (3)	52.0±0.9[a] 51.9±1.0	52.9±0.5[a] 54.2±0.3
	T-matM revised	49.2±1.1	47.8±0.5[a]	51.7±1.1[a] 51.4±0.8
Relative doses	MinR	1.0	0.56/0.70[a]	1.3[a]
	OMI	0.51	0.30/0.37[a]	0.49/0.59[a]
	T-matM revised	0.31	0.25[a]	0.28/0.36[a]

[a] Results in Kodak MinR cassettes; others in envelopes.
Mean difference: envelope − cassettes *in this series* = −0.1 and mean dose ratio: cassette/envelope *in this series* = 1.20.
Results are means with standard errors and numbers of sets of films (six films per set) are given in brackets.

screens. It is understood that the original supplies were withdrawn by the makers, and the film reported here is an improved version. A supply of OMI film was also obtained and tried because of its considerable popularity and in spite of its relatively poor performance in previous work (Kirkpatrick & Law, 1987).

The results are given in Table I. When MinR film was used with MinR fast screens; two sets of films were obtained with the film emulsion facing the back and the front screens. The mean image scores were identical in the two sets.

Fuji products

Fresh samples of Hi-Mammo screens and NH film were obtained, since these had performed well in the preceding comparison series. One new film (Fuji MA) was also obtained. Results of comparisons within this group and with MinR films and screens are given in Table II. These screens, and NH film, were also used on selected products of other manufacturers and the results are shown in Table III. In this work, seven different Hi-Mammo screens were used, and several different boxes of NH film. These screens had not been used in the previous work referred to above. Only one box of MA film was available.

Table II. Image scores and relative doses for Fuji products and Kodak MinR

	Film	Screen	
		MinR	Fuji Hi-Mammo
Image scores	MinR	55.8±0.3 (9)	56.5±0.5 (2)
	Fuji NH	53.9±0.6 (2)	57.2±0.4 (3)
	Fuji MA	54.0±0.5 (2)	55.5±0.4 (2)
Relative doses	MinR	1.00	1.00
	Fuji NH	0.41	0.44
	Fuji MA	0.44	0.45

Results are means with standard errors, and numbers of sets of films (six films per set) are given in brackets.

Table III. (a) Image scores and relative doses for various films (with screens as stated)

Film	Screen	Image score	Relative[a] dose
Konica	MinR	53.3±0.5	0.37
	Fuji Hi-Mammo	53.6±0.6	0.36
	Konica	52.3±0.5	0.37
	MinR	54.3±0.4	0.51
CEA	Fuji Hi-Mammo	55.9±0.4	0.54

(b) Image scores and relative doses for various screens (with films as stated)

Screen	Film	Image score	Relative[a] dose
Siemens	MinR	56.4±0.4	0.94
Orthex MA	Fuji NH	55.3±0.7	0.44
Konica	MinR	54.9±0.5	0.95
	Fuji NH	52.5±0.4	0.42
	Konica	52.3±0.5	0.37

[a] Relative to 1.00 for MinR–MinR.

Agfa products

One fresh type of film and screen were provided. The film was understood to be MR5, but the screen was given no identifying name, and it is now understood that Agfa have withdrawn both, pending fresh developments. These samples performed considerably better than previous Agfa products (except for Medichrome blue), but did not match MinR–MinR or some other combinations. Having been withdrawn at an early stage, they have not been included in tables of results.

Other miscellaneous products

One mammography film and one screen type were obtained from Konica. The Siemens mammography screen, Orthex MA, and film from CEA, were also obtained. Each was tried with MinR screens and films and with a small selection of others which had already scored well. Results are given in Table III.

Discussion

Relative doses

In previous work, relative dose values were rounded to 0.1 or 0.05, this being as precise as the uncertainties in the estimates appeared to allow. In the present work, the consistency of performance in this respect has encouraged us to quote relative doses without rounding.

Kodak products (Table I)

In previous work, OMA film did not perform at all well in image quality. That film is understood to be very similar but not identical to the OMI now supplied. The OMI performed considerably better in this work than the OMA did previously (and at about the same dose), but still did not match MinR in image quality. Moreover, in concurrent but separate work in another screening centre for which Edinburgh is the quality assurance reference centre, a mean difference in image score of 2.6±0.6 was found between OMI and MinR films, OMI being the lower. That work used two X-ray sets and one processor, all different from those in the present work. The OMI film cannot, therefore, be recommended in preference to MinR, and appears to be at least equalled by several other films (Table IV) at similar doses.

T-matM is a double-sided film and certainly the fastest film in this series, but it also gives the poorest image quality. This tendency for reduced dose to be accompanied by poorer image quality has been observed before, and might be anticipated as a general rule.

Of the new Kodak screens, neither shows any image quality improvement over MinR. It seems strange that on all three films, both single and double emulsion types, the "fast" screens appear slower than the "medium" screens, and also that, between these two, the double screen should give better image quality than the single type.

In previous work, Kodak cassettes have consistently given poorer image quality than evacuated envelopes, but that is not shown in this work where, on average over four sets of films in Table I, the difference is negligible. It is presumed that this is due to better film–screen contact in the newest cassettes. In the concurrent work at another centre already referred to, a mean difference in image score of 1.2±0·6 was observed between envelopes and cassettes, about half the difference previously observed, the envelopes again being the better. Difference in film–screen contact is the only reason which can be offered to account for this.

Fuji products (Table II)

The result with Fuji NH film and Hi-Mammo screens agrees with results reported previously (Law & Kirkpatrick, 1989). The better image quality obtained with this combination, compared with MinR–MinR, has now been demonstrated on four different X-ray sets and four different processors using between them three different chemistries. The improvement is not a large one, but it is accompanied by a reduction in dose to less than half that required with MinR–MinR. The relative dose reported here of 0.44 is less than the 0.55 reported earlier and is probably more reliable.

The superior performance of NH film compared to MinR is confined to its use on Hi-Mammo screens. On all other screens referred to in Tables I and III(b) MinR performs rather better, though at just over double the dose in every case.

Table IV. Film–screen combinations in order of image score and with relative doses

Film	Screen	Image score	Relative dose
Fuji NH	Fuji Hi-Mammo	57.2±0.4 (3)	0.44
MinR	Fuji Hi-Mammo	56.5±0.5 (2)	1.00
MinR	Siemens Orthex MA	56.4±0.4	0.94
CEA	Fuji Hi-Mammo	55.9±0.4	0.54
MinR	MinR	55.8±0.3 (9)	1.00
Fuji MA	Fuji Hi-Mammo	55.5±0.4 (2)	0.45
Fuji NH	Siemens Orthex MA	55.3±0.7	0.44

Results are means with standard errors, and numbers of sets of films (6 films per set) are given in brackets.

Fuji MA film gave results very similar to NH; the apparent 5% difference in speed is probably not significant. In image quality it shows no appreciable improvement on NH film with any screen, and failed to match the performance of the latter on Hi-Mammo screens.

Since this work was carried out, Fuji have withdrawn the Hi-Mammo screen. They did so although they knew of the favourable results to be reported here, and apparently regardless of increased orders. They have replaced it with a new product, the HR "Fine" screen. Preproduction samples of this which were supplied to us proved to be inferior to the Hi-Mammo screens. As yet there is insufficient data to form a judgment of the final version of this product.

Other products (Table III)

The Konica film, both on the Konica screen and on two others, did not perform particularly well. Again, dose can be reduced at the cost of image quality. The Konica screen did best on MinR film but did not match MinR screens and required almost the same dose. The CEA film performed moderately well, and was best on Fuji Hi-Mammo screens, but on each screen tried it did not match the best film, though doses were comparable.

The Siemens Orthex MA screen also appears to be among the best screens, though not quite matching the Fuji Hi-Mammo type. Two screens were supplied. Their speed is very similar to the others.

General comments

Film–screen combinations giving the best image scores are listed in Table IV, in image score order, and with relative doses also stated. The differences in image score between many of the entries in this table are certainly not significant. Similarly, the relative doses fall into two distinct groups, and a difference between, for instance, 0.44 and 0.54 probably ought not to influence a choice unless no other criterion can be found.

Several combinations now appear possibly better than MinR–MinR, but most of these involve the Fuji Hi-Mammo screen. With the withdrawal of this useful product, and in the absence of sufficient data on the replacement HR Fine screen, there are few acceptable alternatives to MinR–MinR which also give a lower dose, but the Siemens Orthex MA screen does seem worth further consideration.

Of the films, MinR still achieves the most entries, but at doses now beginning to look on the high side. With increasing use of magnification techniques and loading limits on the associated fine foci, a faster film–screen combination is desirable for this reason as well as for dose reduction. Fuji NH appears to perform better with a background density of 1.1 to 1.3 than at around 0.9, whereas MinR is less sensitive in this respect.

Users considering changing from MinR film should note that in subjective appearance MinR film is clearly less grainy or noisy than any other film discussed here. The smooth appearance of the films may be more noticeable under the detail-free regions of a phantom than ever it is on a clinical mammogram. This same smooth appearance may also contribute to an impression of "flatness", which may be compared unfavourably with the apparent "sparkle" or "brightness" of some other films. Users should be aware of this aspect of choosing a film, and give it no more than its due weight.

Cassettes in comparison with envelopes

In previous work (Law & Kirkpatrick, 1989), cassettes were sometimes found to give considerably poorer image quality than envelopes, but this did not apply to those with carbon fibre fronts or to the Dupont Cronex type. These remarks apply only when the same screens and films are used in both envelopes and cassettes.

In an earlier paper (Kirkpatrick & Law, 1987) Kodak cassettes were reported to give inferior image quality compared with envelopes, possibly because of poorer film–screen contact, and the present work supports that interpretation. When very new, or with adequate screen backing, Kodak cassettes may be entirely satisfactory in this respect.

Fuji cassettes have been compared with envelopes, both during this work and previously, using at least three different film–screen combinations, and no significant difference was observed. These cassettes have carbon fibre fronts.

Conclusion

With the surprising withdrawal of the Fuji Hi-Mammo screens, there are once again few recommendable alternatives to the well tried MinR–MinR combination, if image quality is the prime consideration. There are none if at the same time an appreciably lower dose is also required. In choosing a film–screen combination for use over a number of years it seems necessary to ask the manufacturer, especially in respect of the screens, whether they will remain in production for a reasonable period. It is also worth noting that many manufacturers modify their products at least slightly without altering the product name. This makes long-term objective and quantitative monitoring of image quality of the first importance.

References

KIRKPATRICK, A. E. & LAW, J., 1987. A comparative study of films and screens for mammography. *British Journal of Radiology*, *60*, 73–78.

LAW, J., FAULKNER, K. & SMITH, S., 1989. Measurement of X-ray tube potential in the mammographic region. *Physics in Medicine and Biology*, *34*, 717–725.

LAW, J. & KIRKPATRICK, A. E., 1989. Films, screens and cassettes for mammography. *British Journal of Radiology*, *62*, 163–167.

WHITE, D. R. & TUCKER, A. K., 1980. A test object for assessing image quality in mammography. *British Journal of Radiology*, *53*, 331–335.

1990, *The British Journal of Radiology*, *63*, 132–134

Case reports

Bilateral pneumothorax as a presenting feature of metastatic angiosarcoma of the scalp

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Angiosarcoma of the scalp is a rare highly malignant tumour which frequently metastasizes to lung (Holden et al, 1987). Here we report a case of bilateral pneumothorax in a man with apparently localized angiosarcoma of the scalp. This case illustrates the need to be aware of the aggressive nature of this tumour and to suspect metastases when pulmonary complications develop.

Case report

In June 1988, a 77-year-old man presented with a 6 week history of an enlarging lesion on his scalp. On examination, there was a 3 cm diameter pink-purple nodule with several smaller satellite lesions extending for a further 1 cm. There were no palpable lymph nodes. A biopsy of this lesion showed it to be an angiosarcoma. The scalp lesion was completely excised and the area grafted. The histology of the excised lesion confirmed an angiosarcoma which was completely excised but close to the deep excision line. Within 1 month of the surgery he developed a local recurrence and he was referred for radiotherapy. Before this began however, he was admitted as an emergency with a large spontaneous right pneumothorax. There was no evidence of any metastases on his chest radiograph but on examination he did have an obvious recurrence of his angiosarcoma which had begun to ulcerate. The pneumothorax was managed with immediate insertion of an intercostal chest drain which resulted in partial reinflation of the right lung. However, 2 days later he developed a pneumothorax on the left side and this required insertion of an intercostal drain. The left chest drain was removed after satisfactory reinflation of the lung, but the right side required a pleurodesis. Twenty-four hours after this procedure the left lung collapsed again and a further intercostal drain was inserted on this side. The left lung reinflated satisfactorily, but the patient's general condition rapidly deteriorated and he died the following day.

At post-mortem examination there was no macroscopic evidence of tumour in the lungs, but there were emphysematous bullae in both lungs and haemorrhagic areas on the pleura. However, on microscopic examination there was angiosarcoma in the lung parenchyma and on the pleural surfaces. Several of the haemorrhagic areas in the visceral pleura were adjacent to bullae. There were no metastases at other sites in the body. It was therefore concluded that the angiosarcoma might have caused rupture of the bullae, thereby explaining the bilateral pneumothorax.

Discussion

Angiosarcomas account for less than 1% of all sarcomas. Approximately one third of cases occur in the skin, one third in soft tissues and one third in other sites including breast, liver and bone (Enzinger & Weiss, 1983). Cutaneous angiosarcomas occur most commonly on the face and scalp of elderly patients but are also seen in association with chronic lymphoedema, as first described by Stewart and Treeves in 1948. Angiosarcomas of the face and scalp behave aggressively with local persistence of tumour and spread into soft tissues and distant metastases in a high proportion of patients. The majority of these patients are elderly and their prognosis is poor. In the series by Holden et al, only 12% of patients survived 5 years or more.

On macroscopic examination angiosarcomas of the skin appear as ill-defined haemorrhagic areas. They widely infiltrate the dermis and characteristically extend beyond their macroscopic margins. The tumour is made up of vascular channels which may be irregular or well defined. In contrast to benign vascular tumours, the channels tend to communicate with each other and dissect through normal dermal structures and across fascial planes. The cells lining the vascular spaces are enlarged and have hyperchromatic nuclei. They may appear heaped up and mitotic figures can be identified. Ultrastructural similarities to normal endothelium are variable. Immunohistochemical marking by Ulex europaeus facilitates identification but Factor VIII-AG is variable. Other monoclonal antibodies are being developed with greater sensitivity and specificity.

Osteosarcomas are thought to be the most common metastatic tumour causing "spontaneous pneumothorax" (D'Angio & Iannoccone, 1961), but there are numerous reported cases with other types of tumours. In one series of 33 patients with angiosarcoma of the scalp described by Kitagawa et al (1987), pneumothorax was reported in 11% of patients. This relatively high incidence was not found in the series of patients studied by Holden et al, nor in the other large series by Enzinger and Weiss (1983). There have, however, been other case reports of pneumothorax in angiosarcoma of the scalp (Kitamura & Tamura, 1978) and one case of bilateral pneumothorax in metastatic angiosarcoma of the breast

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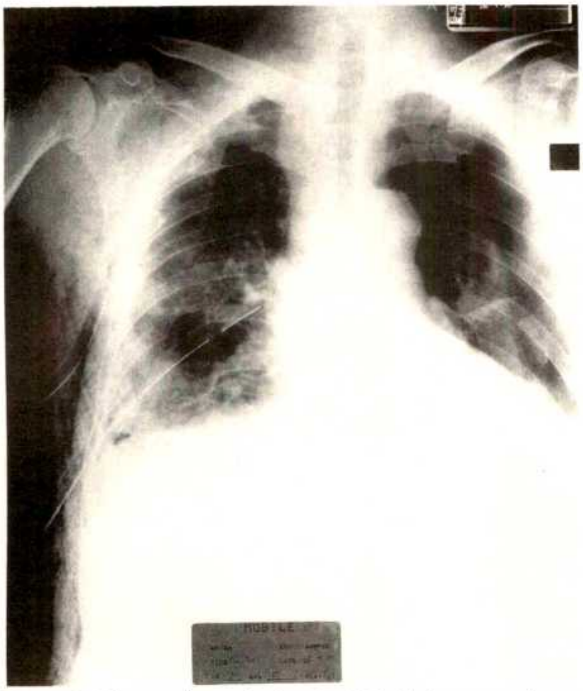

Figure 1. Chest radiograph showing left-sided pneumothorax and reinflated right lung with an apical and a basal chest drain following pleurodesis.

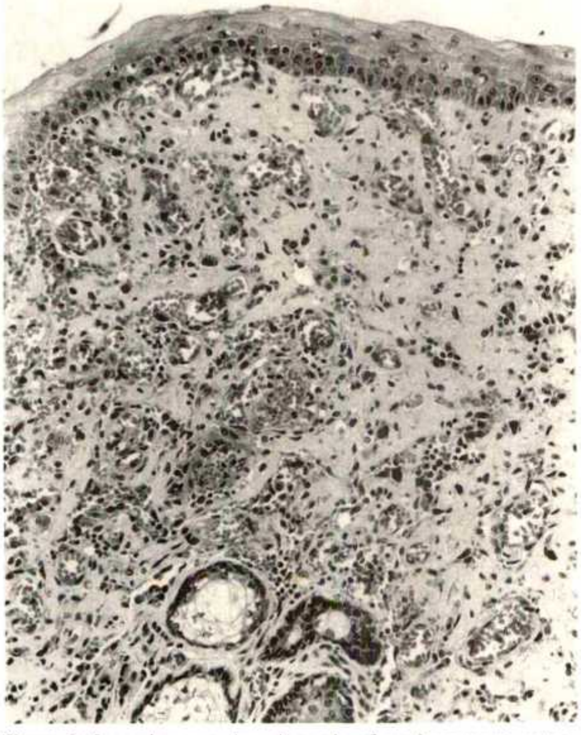

Figure 2. Irregular vascular channels of angiosarcoma extensively invading dermis. The lining cells are pleomorphic and have hyperchromatic nuclei (× 100).

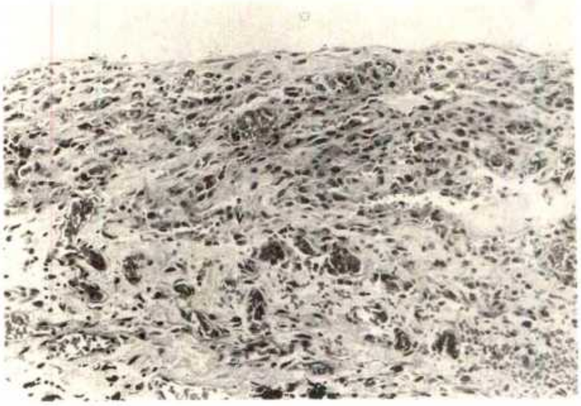

Figure 3. Visceral pleura showing diffuse infiltration by angiosarcoma (× 100).

(Kader et al, 1987). Interestingly, Kitagawa et al did not find any cases of pneumothorax in the 62 cases of angiosarcoma which occurred at sites other than the scalp. One possible explanation for this is the high incidence of pleural and subpleural deposits in cases of angiosarcoma of the scalp. The common feature to all the reported cases is an extremely poor survival following the development of lung complications.

The optimum treatment advocated for scalp angiosarcoma by Holden et al is radiotherapy with an electron beam to the tumour site and surrounding skin. It is necessary to give a generous margin around the tumour as it usually extends beyond its macroscopic boundary and marginal recurrences are common. Radical doses are needed for the local control of tumour and doses between 44 Gy and 60 Gy, given over 4 and 6 weeks respectively and with 4 fractions a week, have been followed by long-term control of local disease. Surgery should be considered for small lesions and the rate of local recurrence may be reduced by radiotherapy to the tumour margins. Two of the patients treated with radical radiotherapy in this series developed pulmonary metastases 10 years later with no sign of recurrence at the primary site. This suggests that the local control of tumour may not necessarily correlate with improved survival. Despite this, it is important to try to achieve local control of the primary tumour as persistent local disease can be unpleasant and disfiguring.

Intensive chemotherapy is mostly inappropriate for this elderly group of patients and there is little evidence that it improves the outcome. Pulmonary complications should be managed symptomatically with awareness of the likely poor prognosis. This case with bilateral pneumothorax illustrates the aggressive nature of this tumour and evidence is given that subpleural deposits may lead to a pneumothorax. In such cases, as with ours, a pneumothorax may be the only evidence for metastatic disease.

References

D'Angio, G. J. & Iannocone, G., 1961. Spontaneous pneumothorax as a complication of pulmonary metastases in malignant tumours in childhood. *American Journal of Roentgenology*, *86*, 1092–1102.

Enzinger, F. M. & Weiss, S. W., 1983. Soft tissue tumours (Mosby, St. Louis, USA), pp. 422–462.

Holden, C. A., Spittle, M. F. & Wilson Jones, E., 1987. Angiosarcoma of the face and scalp, prognosis and treatment. *Cancer*, *59*, 1046–1057.

Kader, H. A., Bolger, J. J. & Goepel, J. R., 1987. Case report: bilateral pneumothorax secondary to metastatic angiosarcoma of the breast. *Clinical Radiology*, *38*, 201–202.

Kitagawa, M., Tanaka, T., Matsubara, O. & Kasuga, T., 1987. Angiosarcoma of the scalp: report of two cases with fatal pulmonary complications and a review of Japanese autopsy registry data. *Virchows Archiv*, *412*, 83–87.

Kitamura, K. & Tamura, N., 1978. Malignant angioendothelioma of the skin. A report of three cases showing lung metastasis and pneumothorax. *Keio Journal of Medicine*, *27*, 123–134.

Stewart, F. W. & Treeves, N., 1948. Lymphangiosarcoma in postmastectomy lymphoedema: a report of 6 cases in elephantiasis chirurgica. *Cancer*, *1*, 64–81.

Pelvic actinomycosis: beware the intrauterine contraceptive device

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Actinomycosis of the abdomen and pelvis is known as "the great imitator" because of its varied clinical presentations. This, together with its rarity, makes its diagnosis difficult. We present two cases of pelvic actinomycosis in females with intrauterine contraceptive devices (IUCD) *in situ*, and stress the need to consider this diagnosis when pelvic neoplasia or inflammatory disease are suspected.

Case report

Case 1

A 46-year-old female was admitted with a 4 day history of colicky lower abdominal pain, diarrhoea, anorexia, "anal lumps" that were rapidly enlarging and recent weight loss. There was no noteworthy past medical history. An IUCD (Saf-T) had been in place for 15 years. Abdominal examination revealed a firm, fixed, tender lower abdominal mass that was palpable on vaginal and rectal examinations. The cervix appeared normal. A provisional diagnosis of pelvic malignancy was made.

Ultrasound examination was performed and the IUCD was noted within the uterus (Fig. 1). The adnexae and outlines of the uterus were obscured and hypoechoic areas around the uterus were thought to represent fixed bowel loops. A discrete mass could not be demonstrated. Examination under anaesthesia revealed a fixed pelvis. Sigmoidoscopy was performed, but the scope could not be passed beyond 10 cm. The rectal mucosa appeared normal. The IUCD was removed and dilatation and curettage performed. A computed tomographic (CT) scan (Fig. 2) showed generalized soft-tissue thickening throughout most of the pelvis with obliteration of the tissue planes around the rectum, uterus and posterior aspect of the bladder. Gastrografin-filled narrowed bowel was demonstrated within this "mass" and several small gas pockets were noted. These findings were consistent with pelvic malignancy.

At surgery, the small- and large-bowel loops were matted together within the pelvis. The uterus was a little bulky and fixed to the bladder. After division of adhesions, the pouch of Douglas was entered. Marked fibrosis was evident, especially around the recto-sigmoid junction. The ovaries appeared normal as did the liver, para-aortic regions, kidneys and omentum. Multiple biopsies were taken from various sites. Both ovaries and fallopian tubes were removed and a temporary colostomy performed.

Histology showed a florid chronic granulomatous inflammation involving both ovaries and tubes. Several sulphur granules were evident and in this clinical context indicated actinomycosis infection. There was no evidence of neoplasia or endometriosis. Stains for bacteria, tuberculosis and other fungi were negative. The patient was placed on high-dose penicillin and has made a steady progressive recovery. A follow-up CT scan performed at 5 months (Fig. 3) showed considerable overall improvement.

Case 2

A 28-year-old female with a 6 week history of vague lower abdominal pain presented with an acute severe exacerbation with vomiting, requiring emergency laparotomy. There was no noteworthy past medical history and she was not on medication. An IUCD was in place. At surgery, a localized area of severe inflammation was found around the lower sigmoid colon. A defunctioning colostomy was performed and she was commenced on metronidazole and cephalosporins.

An area of extrinsic narrowing was shown on subsequent barium enema and sigmoidoscopy (Fig. 4), but no diverticula were demonstrated. Although there was some improvement, she never completely recovered and complained of continuing vague discomfort and lower abdominal pain. A further barium enema showed resolution of the stricture and no evidence to suggest diverticular or Crohn's disease. The distal ileum was also demonstrated and had normal appearances at this time. She was thought to have spastic colon. She represented 7 months later feeling generally unwell, and with intermittent pyrexia. She complained of left iliac fossa pain, diarrhoea and dysuria, all increasing in severity over 3 weeks. Examination revealed a vague lower abdominal mass and tenderness. She was found to be mildly anaemic with an elevated white cell

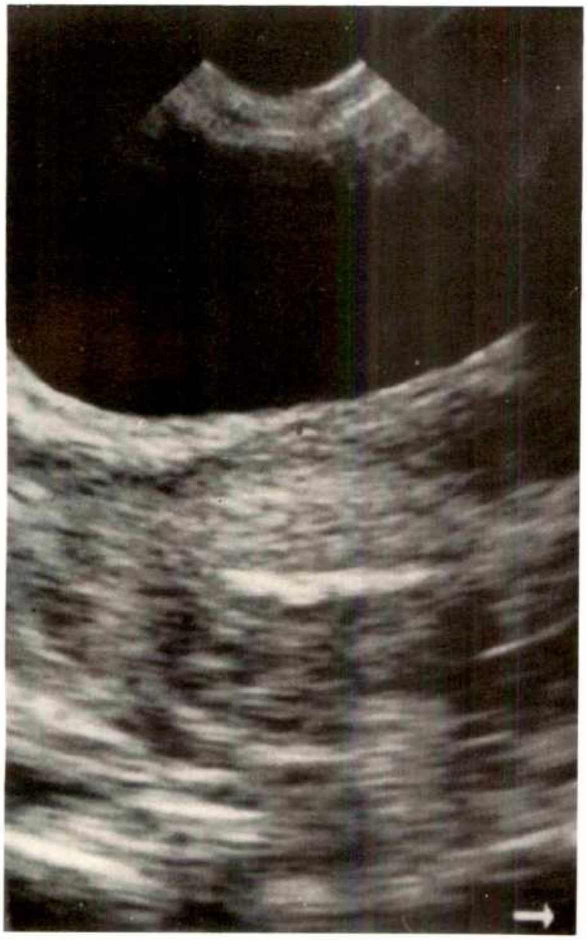

Figure 1. Longitudinal ultrasound scan shows the hyper-reflective IUCD within the uterus, the margins of which are ill defined.

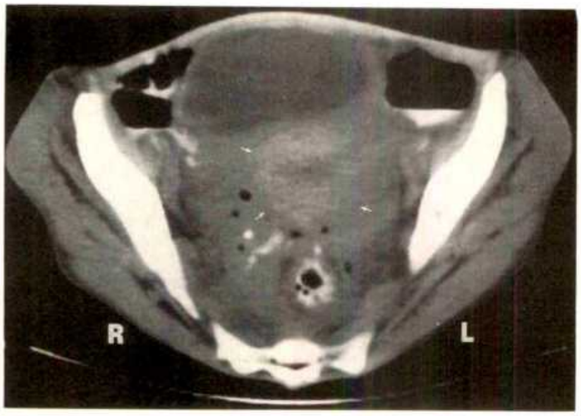

Figure 2. Computed tomographic scan of the pelvis demonstrates generalized thickening with loss of the tissue planes. Gastrografin is present in the rectum and a loop of small bowel. The gas pockets were thought to be within the bowel, although an abscess could mimic these appearances. The uterus is marked by the arrows.

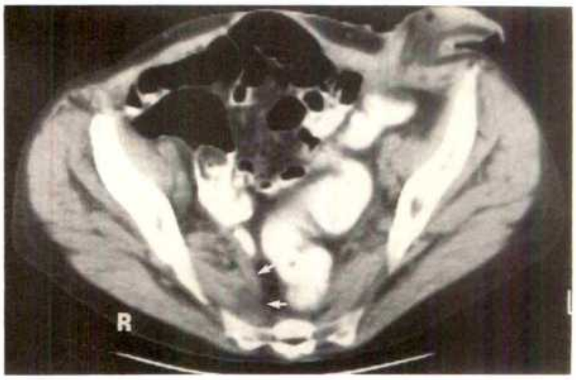

Figure 3. Computed tomography shows considerable resolution with reappearance of the tissue planes. Note some residual tissue thickening on the right (arrows).

count and erythrocyte sedimentation rate (ESR). Ultrasound revealed an IUCD within a swollen uterus but no adnexal mass. An intravenous urogram (IVU) revealed right ureteric obstruction just above the pelvic inlet. There was no significant growth from cervical swabs or urine cultures. She was placed on tetracycline for her presumed pelvic inflammatory disease, but response was poor. Laparotomy was performed to confirm the diagnosis and to drain a possible abscess. An indurated frozen pelvis was found with no evidence of malignancy. The IUCD was removed. Cultures from various sites revealed mixed growths. Broad spectrum, long-term antibiotic treatment was commenced but with little improvement.

Three months later an abscess developed in the right groin. This was incised, and culture grew actinomycosis israeli. The patient was placed on high-dose penicillin for several months which resulted in a dramatic improvement with weight gain and relief of symptoms. However, a repeat IVU 5 months later showed further deterioration of right renal function and a residual pelvic mass. This has been treated conservatively.

Discussion

Actinomycosis israeli, "the ray fungus", is a common saprophyte found in the mouth, throat and intestines of

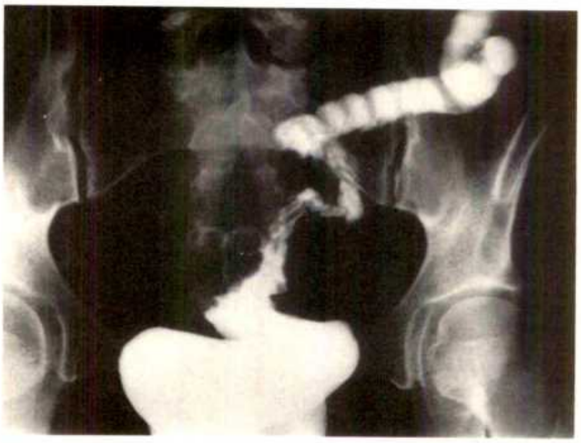

Figure 4. Barium enema shows a stricture of the lower sigmoid colon; note the IUCD.

normal humans. Although not normally found in the vagina, it has been isolated in up to 25% of females with IUCDs, although it is rarely symptomatic. The fungus is unable to penetrate intact mucosa and as a result only rarely acts as a pathogen. It is an opportunistic organism: intestinal perforation, previous surgery, trauma, dental caries, neoplasia, diverticula disease, cholecystitis, appendicitis, steroid therapy, diabetes mellitus and the presence of a foreign body are all predisposing factors to the development of this infection (Harvey et al, 1967; Davies & Keddie, 1973; Gingold & Fazio, 1978; Beradi, 1979). The abdomen and especially the ileo-caecal region is the most frequent site of infection after the head and neck (Davies & Keddie, 1973). The female genital organs are only rarely involved but, when present, tubo-ovarian infection is the most common site. Although direct spread from the gastrointestinal tract is considered to be the usual route of infection, it seems likely that vaginal organisms are the source of infection in at least some of the cases associated with IUCDs.

Actinomycosis of the abdomen or pelvis is a rare disease with a wide spectrum of clinical presentation and, as a result, the diagnosis is made preoperatively in less than 10% of cases (Weese & Smith, 1975). The infection usually presents as a subacute or chronic illness, with a variety of symptoms including pain, constipation or diarrhoea, leukorhoea, menorrhagia, amenorrhoea, dysuria, pyrexia, fatigue, malaise and weight loss. Anaemia and leukocytosis may be present and ESR is nearly always elevated (Surur, 1974). Neoplasia, inflammatory bowel disease and infection are included in the differential diagnoses.

There are no specific radiological features of pelvic actinomycosis, the findings reflecting the pathological processes involved (Fowler & Simpkins, 1983). Fluoroscopy, ultrasound and CT may demonstrate a discrete mass or a diffuse thickening of the tissues, as in Case 1. Multiple abscess cavities usually develop as the central areas of the granulomatous mass liquify; sinus tracts and fistulae often ensue. Direct spread occurs across tissue planes helped by the action of proteolithic enzymes released by the organisms. These appearances are, however, common to both infection and necrotic tumours. Angiographic appearances are often similar in abscesses and infection and are not therefore considered helpful (Olssen, 1974).

Radiology, and particularly CT, may have an important role to play in suggesting the diagnosis, facilitating biopsy and providing an assessment of the patient's response to treatment.

In a review of the recent radiology literature over the past 14 years, there have been 10 reported cases involving the abdomen or pelvis, and four of these had a history of IUCD *in situ* (Surur, 1974; Fowler & Simpkins, 1983; Maloney & Cho, 1983; Roesler & Wills, 1986; Shah et al, 1987). Our cases both had IUCDs in place. It seems that the association between pelvic actinomycosis and the presence of an IUCD is becoming increasingly important. The time between insertion of the IUCD and development of infection is variable, but is more frequently seen in women with the device having been in place for many years. The increased incidence of pelvic inflammatory disease in general, associated with the use of IUCDs, is well recognized. It is worth noting that many authors believe that actinomycosis in any site rarely occurs in isolation but is usually associated with infection with other organisms.

Definite diagnosis of actinomycosis requires culture of the fungus. More often the diagnosis is made by means of histological demonstration of sulphur granules and although these may be seen in other fungal infections they may be taken as diagnostic for actinomycosis in the appropriate clinical setting (Shah et al, 1987) as in Case 1. The granules are sparse and this explains why they are not always demonstrable on aspiration or biopsy specimens. The likelihood of a successful culture is enhanced if the diagnosis is suspected as microaerophilic and anaerobic cultures are required. Also, prior antibiotic treatment decreases the chances of successful growth.

Actinomycosis is nearly always sensitive to penicillin, but prolonged treatment for up to several weeks after all evidence of infection has cleared is necessary to decrease the chances of recurrence. Surgery is only occasionally required to clear the infected tissues and organs, to drain a resistant collection or, as in our case, to relieve obstruction. The role of percutaneous catheter drainage is not known.

Fowler and Simpkins (1983), among others, have stressed that a rapidly enlarging mass, fixation of the mass, sinus tract or fistulae formation should suggest the diagnosis.

In summary, we have described two cases of pelvic actinomycosis, both associated with the presence of an IUCD. We wish to stress the need to consider actinomycosis when the radiological features suggest either pelvic malignancy or infection in a patient with recent history of IUCD use.

Acknowledgments

We would like to thank Miss Miller for permission to report on Case 1 and Dr R. Thind for allowing access to the ultrasound study in Case 1.

References

BERADI, R. S., 1979. Abdominal actinomycosis. *Surgery, Gynaecology and Obstetrics, 149*, 257–266.

DAVIES, M. & KEDDIE, N. C., 1973. Abdominal actinomycosis. *British Journal of Surgery, 60*, 18–22.

FOWLER, R. C. & SIMPKINS, K. C., 1983. Abdominal actinomycosis: a report of three cases. *Clinical Radiology, 34*, 301–307.

GINGOLD, B. S. & FAZIO, V. W., 1978. Abdominal actinomycosis: a complication of colonic perforation. *Diseases of the Colon and Rectum, 21*, 374–376.

HARVEY, J. C., CANTRELL, J. R. & FISHER, A. M., 1957. Actinomycosis: recognition and treatment. *Annals of Internal Medicine, 46*, 868–885.

MALONEY, J. J. & CHO, S. R., 1983. Pelvic actinomycosis. *Radiology, 148*, 388.

OLSSEN, T., 1974. Angiography in actinomycosis of the abdomen. *American Journal of Roentgenology, 122*, 278–280.

ROESLER, P. J. & WILLS, J. S., 1986. Hepatic actinomycosis: CT features. *Journal of Computer Assisted Tomography*, *10(2)*, 335–337.

SHAH, H. R., WILLIAMSON, M. R., BOYD, C. M., BALACHARDRAN, S., ANGTUACO, T. L. & MCCONNELL, J. R., 1987. CT findings in abdominal actinomycosis. *Journal of Computer Assisted Tomography*, *11(3)*, 466–469.

SURUR, F., 1974. Actinomycosis of female genital tract. *New York State Journal of Medicine*, *74*, 408–410.

WEESE, W. C. & SMITH, I. M., 1975. A study of 57 cases of actinomycosis over a 30 year period. A diagnostic 'failure' with good prognosis after treatment. *Archives of Internal Medicine*, *135*, 1562–1568.

Unusual appearances of an adrenal mass on computed tomography

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When patients undergo imaging investigations to stage malignant disease the finding of a mass in the adrenal gland may not necessarily represent metastasis. Incidental non-functioning adrenal masses have been reported in 0.6% of examinations of the abdomen by computed tomography (CT) (Glazer et al, 1982). We report a patient with such a finding, whose CT scans showed unusual appearances.

Case report

A 64-year-old Caucasian man with histologically proven adenocarcinoma of the prostate was referred for CT for staging purposes. There were no clinical signs to suggest spread of the disease and no symptoms referable to the abdomen. Prior to this he had been well.

Computed tomography showed moderate enlargement of the prostate with no evidence of periprostatic infiltration or lymphadenopathy. The left adrenal gland was replaced by a large, well circumscribed mass measuring 8 × 9 × 10 cm. The mass was of uniformly high attenuation (83 Hounsfield Units, standard deviation 4.3) apart from a few flecks of overt calcification within it (Fig. 1). Sections taken following an intravenous injection of 100 ml of meglumine diatrizoate 65% (Urografin 310M, Schering) showed no detectable increase in attenuation, indicating that the "mass" was avascular. A normal right adrenal gland was identified.

He was normotensive and a chest radiograph was normal. Serum biochemistry showed no abnormality and there was no elevation of urinary vanillylmandelic acid level.

At CT-guided biopsy, two passes with a Trucut biopsy needle failed to obtain any material. A 14G intravenous cannula (Abbocath, Abbott) was therefore inserted and aspiration revealed pus, 40 ml of which was removed. Cytological examination of this showed necrotic debris and dystrophic calcification. Bacteriological examination showed no pus cells or organisms, including acid fast bacilli. On culture there was a mild growth of *staphylococcus epidermis*, believed to be a contaminant. Cultures for tuberculosis were negative at 6 weeks, but a tuberculin test was strongly positive at a dilution of 1 in 10,000.

A presumptive diagnosis of tuberculous abscess was made and he was started on antituberculous therapy. He underwent a radical course of radiotherapy to the pelvis and remains well 7 months later.

Discussion

To our knowledge, an adrenal mass with these appearances has not been previously reported. Incidental adrenal masses may show evidence of calcification on radiographs, ultrasound or CT in 30% of patients (Kenney & Stanley, 1987). The appearances in our patient were unusual in that although there were tiny flecks of calcification, the mass was otherwise of uniformly high attenuation owing to calcium deposition in chronic suppuration. A previously reported case of unilateral caseous tuberculosis contained no calcification, was of low attenuation and demonstrated ring enhancement (Hauser et al, 1981). None of these features were present in our patient.

Organisms that infect the adrenal glands in adults include tuberculosis, histoplasmosis and blastomycosis as well as pyogenic infections (O'Brien et al, 1987). Granulomatous inflammation usually causes bilateral adrenal gland enlargement, with subsequent atrophy

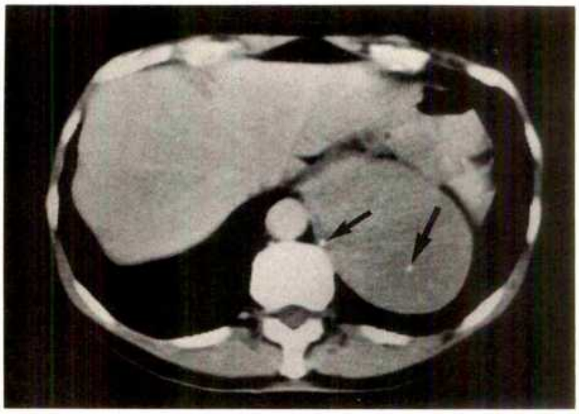

Figure 1. Enhanced CT section of the upper abdomen, showing the left adrenal gland replaced by a well defined mass of high attenuation, containing small areas of calcification (arrows). (W = 300, L = 38.)

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leading to bilateral small calcified glands and sometimes Addison's disease (Wilms et al, 1983). Unilateral disease appears to be uncommon.

The finding of a unilateral adrenal mass in a patient with known malignant disease must always raise the possibility of metastasis. We agree with Bernadino et al (1985) that guided biopsy is indicated in these circumstances, if only to exclude metastasis, as in our patient.

Acknowledgments

We are grateful to Dr C. J. Alcock for his permission to publish clinical details of this patient and to Miss J. Edmonds and Mr S. Ashington for their assistance.

References

BERNADINO, M. E., WALTHER, M. M., PHILLIPS, V. M., GRAHAM, S. D., WHITAKER SEWELL, C., GEDGAUDAS-MCCLEES, K., BAUMGARTNER, B. R., TORRES, W. E. & ERWIN, B. C., 1985. CT guided adrenal biopsy: accuracy, safety and indications. *American Journal of Roentgenology*, *144*, 67–69.

GLAZER, H. S., WEGMAN, P. J., SAGEL, S., LEVITT, R. G. & MCCLENNAN, B. L., 1982. Non-functioning adrenal masses: incidental discovery on computed tomography. *American Journal of Roentgenology*, *139*, 81–85.

HAUSER, H., BOTTIKHA, J. G. & WETTSTEIN, P., 1981. Pathology of the adrenal glands: common and uncommon findings in CT. *European Journal of Radiology*, *1*, 215–226.

KENNEY, P. J. & STANLEY, R. J., 1987. Calcified adrenal masses. *Urologic Radiology*, *9*, 9–15.

O'BRIEN, W. M., CHOYKE, P. L., COPELAND, J., KLAPPENBACH, R. S. & LYNCH, J. H., 1987. Computed tomography of adrenal abscess. *Journal of Computer Assisted Tomography*, *11 (3)*, 550–551.

WILMS, G. E., BAERT, A. L., KINT, E. J., PRINGTO, J. H. & GODDEERIS, P. G., 1983. Computed tomographic findings in bilateral adrenal tuberculosis. *Radiology*, *146*, 729–730.

Magnetic resonance imaging of the chest in infectious mononucleosis

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Infectious mononucleosis is a disease of young adults, typically presenting with malaise, fever, sore throat and cervical adenopathy (Juel-Jensen, 1983). Non-specific respiratory symptoms may also be present. The diagnosis is confirmed by serological tests for the virus.

A case is reported in which the presence of lymphadenopathy as demonstrated by a magnetic resonance imaging (MRI) scan led to the diagnosis of infectious mononucleosis.

Case report

A 12-year-old patient with a 6-year history of asthma (controlled by becotide and ventolin inhalers (Allen and Hanburys)) complained of lethargy and poor appetite following a recent chest infection. On examination, the only abnormality was an enlarged left cervical node.

The chest radiograph (Fig. 1) was normal.

As part of a study of pulmonary disease in childhood, an MRI scan was arranged. The chest was imaged in the coronal plane with T_1-weighted spin–echo (time to repeat (TR) 500 ms, time to echo (TE) 26 ms) and short tau inversion recovery (STIR) (TR 1500 ms T_I 100 ms) pulse sequences. This showed intra- and extra-thoracic lymphadenopathy (Figs 2, 3). The former is seen in the subcarinal and broncho-pulmonary regions; the extra-thoracic lymphadenopathy is present in the left axilla and left supra-clavicular regions. No lung parenchymal abnormality was demonstrated.

The appearances were considered likely to be a result of infectious mononucleosis, lymphoma or sarcoidosis. Other possibilities included "cat-scratch fever" and brucellosis. The

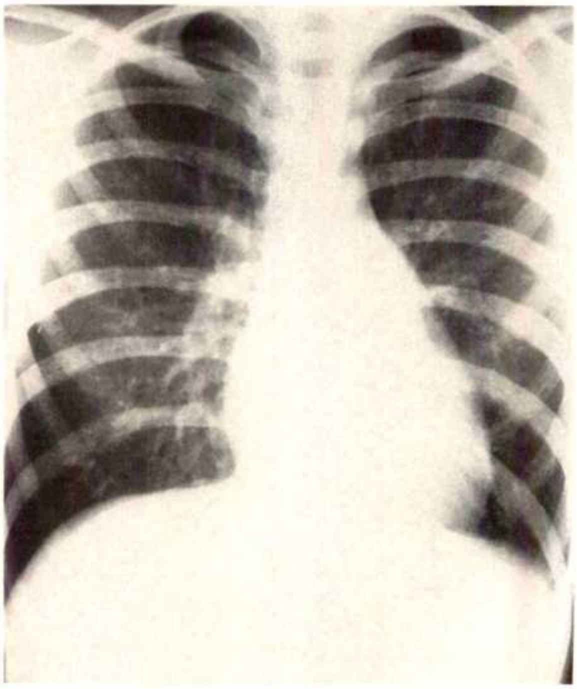
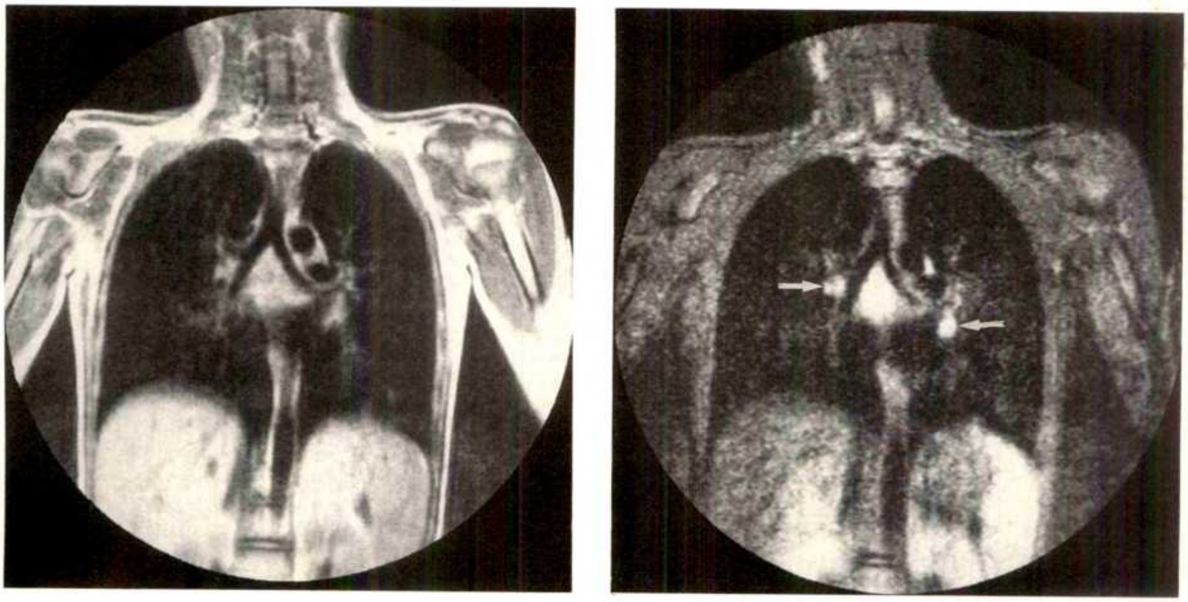


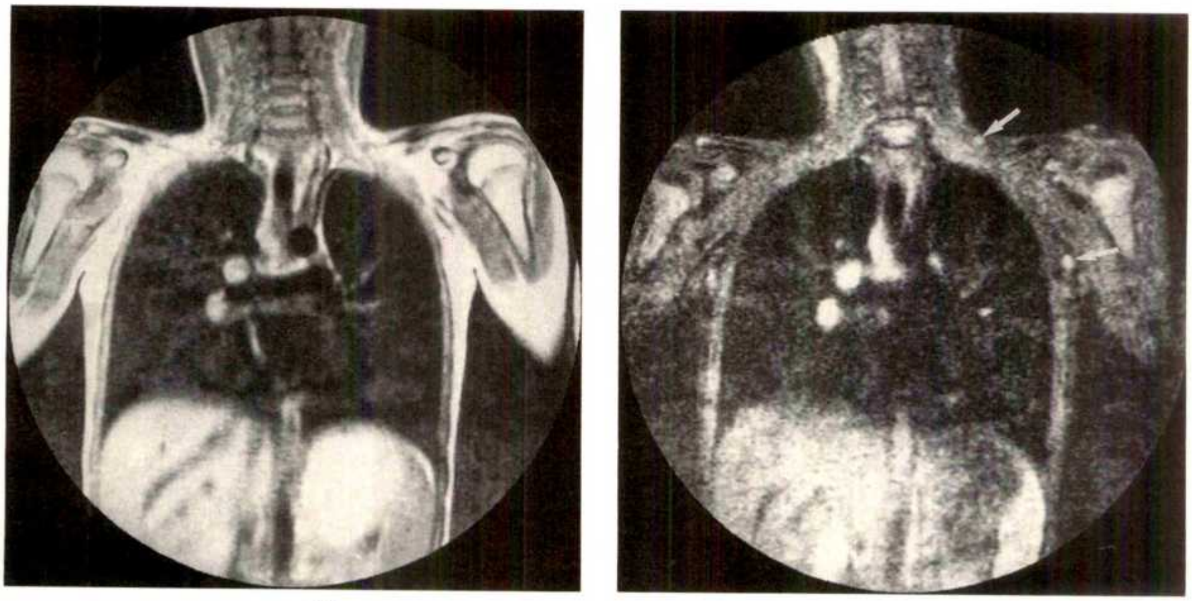
Figure 1. Normal chest radiograph. There is no evidence of hilar adenopathy.



(a) (b)

Figure 2. (a) T_1-weighted and (b) STIR coronal images in the plane of the carina. The high signal of the broncho-pulmonary nodes (arrows) is well shown on the STIR image.

pattern in this case was predominantly of hilar nodal enlargement with other enlarged nodes in the mediastinum, axilla and neck. This pattern would occur in sarcoidosis and infectious mononucleosis, but sarcoid is very uncommon at this age. Lymphoma causes predominantly mediastinal and cervical node enlargement and the hilar component is usually less marked. In "cat-scratch fever", the nodes near to the area of the cat scratch are largest. On balance, infectious mononucleosis was therefore the most likely diagnosis from the MRI scans. Subsequently, the ELISA test for Epstein Barr nuclear antigen and immunofluorescence tests to the virus capsid antibody were found to be positive.



(a) (b)

Figure 3. (a) T_1-weighted and (b) STIR images in a plane anterior to that in Fig. 2. High signal from lymph nodes in the left axilla and left supra-clavicular fossa is seen on the STIR image (arrows). High signal from fat prevents visualization of these nodes on the T_1-weighted image.

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Discussion

The accuracy of MRI in the assessment of hilar and mediastinal lymphadenopathy has been previously described (Gamsu et al, 1983; Goddard, 1987). The coronal T_1-weighted images allow for the precise anatomical location of enlarged lymph nodes not seen on a chest radiograph. This information is important as different disease processes involve different lymph node groups. For instance, sarcoidosis most commonly affects the broncho-pulmonary and right para-tracheal nodes (Cohen et al, 1983). The advantages of MRI over computed tomography in cases of mediastinal and hilar disease are that coronal images are produced and that ionizing radiation is not required. Also, as flowing blood within the vessels produces a signal void, contrast medium injection is not required for vessel identification (Gamsu et al, 1983).

The STIR sequence increases the contrast between tissues with a high water content and surrounding normal tissues (Bydder & Young, 1985). This additional information compensates for the decreased spatial resolution of the STIR sequence; also, as fat gives a high signal on the T_1 images but a low signal on the STIR sequence, it can readily be distinguished from other tissues.

The MRI scans in this case were performed as part of a research protocol. It is not intended that MRI should be performed in all children with recent chest infections and cervical adenopathy or in whom infectious mononucleosis is suspected. However, this case does illustrate the considerable value of MRI in the anatomical localization of mediastinal mass in children.

Acknowledgments

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References

BYDDER, G. M. & YOUNG, I. R., 1985. MR imaging: clinical use of the inversion recovery sequence. *Journal of Computer Assisted Tomography*, *9*, 659–675.

COHEN, A. M., CREVISTON, S., LIPUMA, J. P., BRYAN, P. J., HAAGA, J. R. & ALFIDI, R. J., 1983. NMR evaluation of hilar and mediastinal lymphadenopathy. *Radiology*, *148*, 739–742.

GAMSU, G., WEBB, W. R., SHELDON, P., KAUFMAN, L., CROOKS, L., BIRNBERG, F. A., GOODMAN, P., HINCHCLIFFE, W. A. & HEDGECOCK, M., 1983. Nuclear magnetic resonance imaging of the thorax. *Radiology*, *147*, 473–478.

GODDDARD, P., 1987. *Diagnostic Imaging of the Chest* (Churchill Livingstone, London), pp. 132 and 154.

JUEL-JENSEN, B. E., 1983. Infectious mononucleosis: Epstein-Barr virus disease. In *Oxford Textbook of Medicine* (Oxford Medical Publishing, Oxford), p. 61.

Galactocele of the breast: radiologic and ultrasonographic findings

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A galactocele is a benign lesion of the breast, defined as an encysted collection of milk products. It is usually found in young women during lactation, although it has also been described in girls and men (Vabderschueren-Lodeweycky et al, 1979). The quantity of milk is almost always limited, although an excess may sometimes lead to signs of pressure.

A case of a galactocele is reported, together with its radiological and ultrasound findings.

Case report

A 31-year-old woman presented with a breast mass that had been present for 4 years. She had originally detected this mass during a previous period of lactation, after which she had had a further uneventful pregnancy and had breast-fed for 2 months. During all this time the size of the mass had remained unchanged.

Physical examination revealed a large, smooth mass, 4 cm in diameter and situated in the upper left quadrant of the left breast. The mass was unattached to muscle or skin.

Mammography showed a hypodense mass 4 cm in diameter, with a wall of higher soft-tissue density encompassing small circular components, which had a density greater than the rest of the mass and settled to the bottom when the patient was standing. This latter feature gave the mass an extremely hypodense upper area and a lower area of greater soft-tissue density, separated by an undulating interface (Fig. 1). The appearances were considered to be diagnostic of a galactocele.

Ultrasound showed the mass to contain hypoechoic and highly echogenic portions, separated by a wavy line which tended to remain horizontal in recumbent and erect positions. The mass, which was approximately 37 mm in diameter and was bilobulated, had a highly echogenic, 4 mm wall surrounding highly echogenic images with intense distal acoustic shadowing within its dependent part (Figs 2, 3).

The mass was punctured with a 19-gauge needle and 15 ml of white fluid containing some fatty and some other compact, clotted material was extracted: this proved to be milk. An

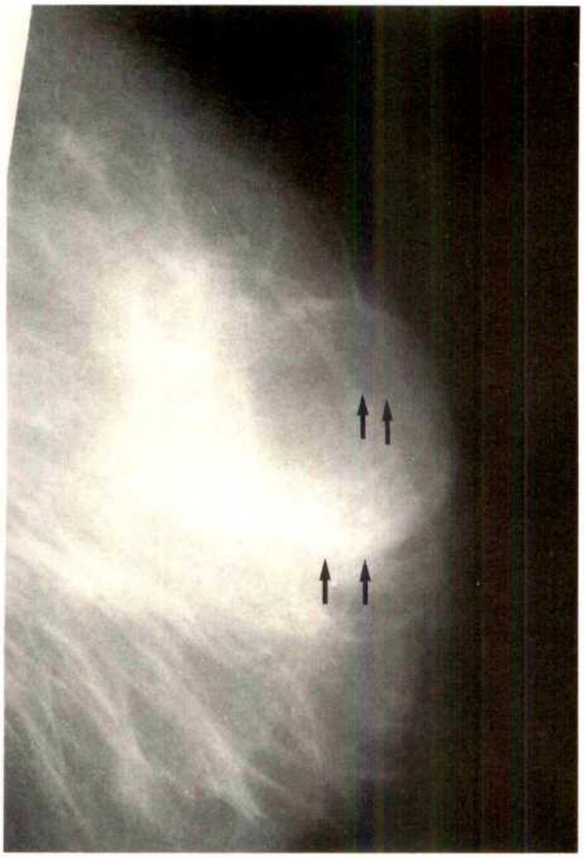

Figure 1. Lateral projection of the left breast, showing a radiolucent mass with the fluid level (upper arrows) separating fluids of fat and low soft-tissue density. A denser deposit has settled in the most dependent part of the cystic mass (lower arrows).

injection of 20 ml of air was given to allow pneumocystography, which revealed a smooth wall and the presence of solid contents that had not been extracted. The patient refused to undergo surgery.

Discussion

The mammographic features of galactoceles have been described in previous reports (Golden & Wangesteen, 1972; Gómez et al, 1986). The appearance of a level separating two different radiological densities, fat and water, is regarded as a pathognomonic finding. While Gómez et al (1986) reported only two densities, Egan (1970) described a similar case to this one in which a further density changed position with patient movement and corresponded to solid contents (Fig. 1), although this galactocele was seen soon after lactation. The density of a galactocele is readily distinguished from that of a cyst containing milk of calcium which has a denser, curvilinear appearance (Sickles & Abele, 1981).

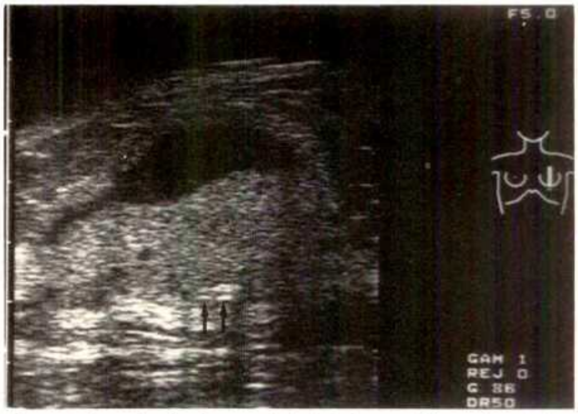

Figure 2. Longitudinal scan of the left breast. The patient is in a supine decubitus position. A cystic cavity with a clearly visible thick wall contains an undulating fluid level separating the upper echolucent and the lower highly echogenic fluids. More highly echogenic images in the posterior area can be seen (arrows) with distal acoustic shadowing.

Although there have been numerous ultrasound studies of breast disorders (McSweeney & Murphy, 1984), the ultrasound findings in galactoceles have not previously been reported in the literature. Ultrasound shows the echo-lucency of the upper fluid and the high echogenicity of the lower component which, together with a radiographic density lower than that of water, represents the fat content of the milk products. The persistence of the line separating both components suggests two non-miscible fluids, with the upper fluid having a lower specific gravity (fat) than the lower (milk). Ultrasound also demonstrated the thick wall of the galactocele which, although not specific, could indicate the long duration of the abnormality. The presence of solid, mobile echogenic contents of greater specific gravity than both fluids, and with distal acoustic shadowing in a fluid-filled cavity, may be considered to be highly suggestive of a galactocele. Furthermore,

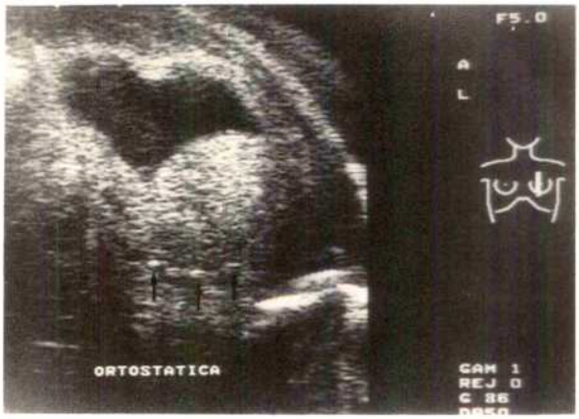

Figure 3. Longitudinal scan of the left breast. The patient is sitting upright: the echogenic images have shifted to the caudal area (arrows) and the fluid level now has a horizontal disposition.

ultrasound demonstrates the waviness of the interface and its tendency towards the horizontal position with patient movement (Figs 2, 3).

References

EGAN, R. L., 1970. *Mammography and Breast Diseases* (Williams & Wilkins, Baltimore, USA), p. 207.

GOLDEN, G. T. & WANGESTEEN, S. L., 1972. Galactocele of the breast. *American Journal of Surgery, 123,* 271–273.

GÓMEZ, A., MATA, J. M., DONOSO, L. & RAMS, A., 1986. Galactocele: three distinctive radiographic appearances. *Radiology, 158,* 43–44.

MCSWEENEY, M. B. & MURPHY, C. H., 1985. Whole-breast sonography. *Radiologic Clinics of North America, 23,* 157–167.

SICKLES, E. A. & ABELE, J. S., 1981. Milk of calcium within tiny benign breast cysts. *Radiology, 141,* 655–658.

VABDERSCHUEREN-LODEWEYCKY, M., GIELEN, M. L., EGGERMONT, E. et al, 1979. Unilateral galactocele in a male infant. *Helvetica Paediatrica Acta, 34,* 617–624.

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Case of the month

Digging for a diagnosis

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(*Received September 1988 and in revised form November 1988*)

A 45-year-old man presented with a 1 week history of progressive painless jaundice. An ultrasound examination at the referring hospital indicated distal common bile duct (CBD) obstruction.

Six years previously he had noticed swelling around both mandibular angles and an orthopantomograph had shown two rounded radio-opaque masses in these areas (Fig. 1). One year later, the patient had a colectomy with an ileo-rectal anastomosis.

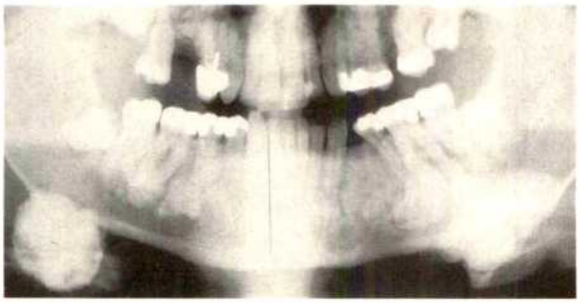

Figure 1. Orthopantomograph of the mandible.

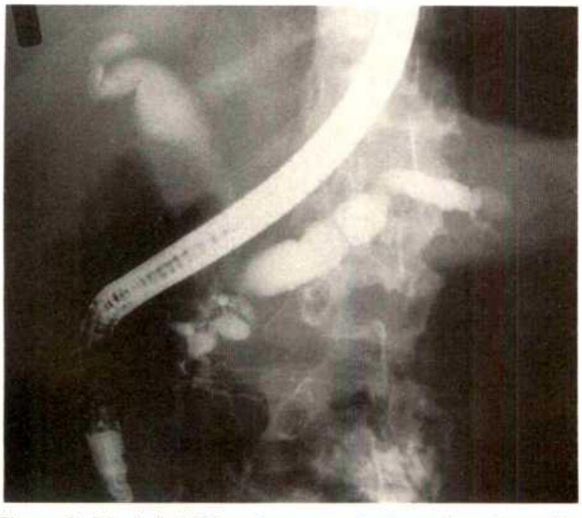

Figure 2. Marked CBD and pancreatic duct dilatation with preservation of pancreatic duct side branches shown by ERCP.

On clinical examination, he was found to be jaundiced, had multiple bony nodules in the region of the chin and forehead with two non-fluctuant, mobile lumps over the occiput and dorsum of the left foot. The liver was smoothly enlarged on palpation. A chest radiograph was normal. Marked CBD and pancreatic-duct dilatation was confirmed on repeat ultrasound and endoscopic retrograde cholangiopancreatography (ERCP) (Fig. 2). A hypotonic duodenogram (Fig. 3) showed multiple, small filling defects in the second part of the duodenum and a 4 cm mass in the region of the ampulla of Vater.

What is your diagnosis?

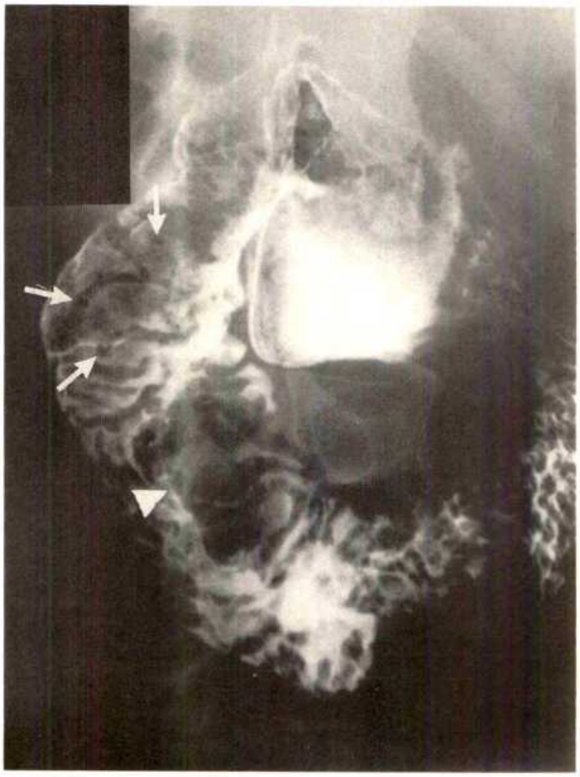

Figure 3. Hypotonic duodenogram demonstrates multiple small filling defects (arrows) and a larger mass in the region of the ampulla (arrowhead).

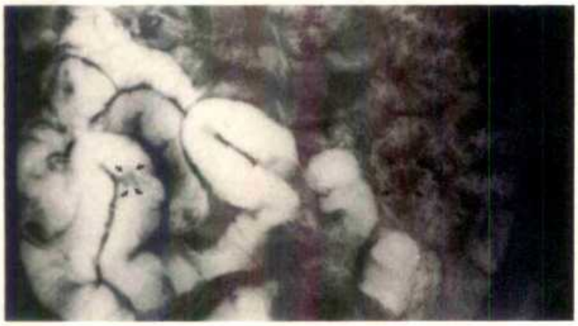

Figure 4. A small bowel follow-through demonstrates multiple polyps in jejenum and ileum (arrows).

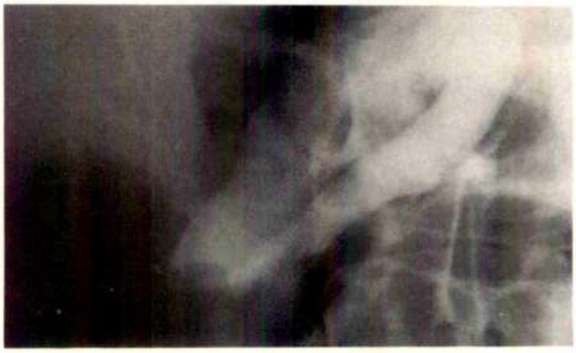

Figure 5. Close-up view of CBD and pancreatic duct confluence showing a mass lesion with irregular margin protruding into and obstructing both ducts.

The diagnosis is Gardner's syndrome, complicated by a periampullary carcinoma.

Our patient had initially presented with two large osteomas of the mandible (Fig. 1). A subsequent barium enema had shown extensive colonic polyposis and led to the diagnosis of Gardner's syndrome. A colectomy had then been performed. Subsequent barium studies of the upper gastrointestinal (GI) tract demonstrated gastric polyps (sparing the antrum), polyps in the duodenum (Fig. 3) and polyps in the jejenum and ileum (Fig. 4). The periampullary lesion seen on the duodenogram was shown to protrude into and obstruct the distal CBD and pancreatic duct on ERCP (Fig. 5).

The patient had a proximal pancreatico-duodenectomy and histology revealed a villous adenoma with a small area of malignant invasion of the muscularis mucosa.

Discussion

Gardner, in 1953 described a syndrome of large bowel polyps with mandibular osteomas and epidermoid cysts as an autosomal dominant inherited disorder (Gardner & Richards, 1953).

Subsequently, numerous other extra-colonic manifestations have been described in the syndrome, including desmoid tumours, mesenteric fibromas, dental abnormalities, upper gastrointestinal and small bowel polyps. The most frequent extra-colonic malignancy is periampullary carcinoma; other less common malignant tumours are papillary carcinoma of the thyroid, medulloblastoma, adrenal carcinoma and carcinoid of the small bowel (Jagelmann, 1987). There is now increasing evidence that Gardner's syndrome and familial polyposis are one entity with the same underlying genetic defect but a variable phenotype (Burt et al, 1984; Jagelmann, 1987).

The polyps in the duodenum tend to be adenomatous (tubular or villous) and must be considered as a premalignant condition unlike gastric polyps, which are of the hyperplastic-fundus-cell type and usually follow a benign course. Duodenal polyps involve, most commonly, the second part of the duodenum and in particular the papilla of Vater. Adenomatous changes can even occur in a papilla that looks macroscopically normal (Burt et al, 1984), or can be confined to the distal CBD and then only be detectable as filling defects on ERCP examination (Shemesh & Bat, 1985).

The reported incidence of periampullary carcinoma in Gardner's syndrome varies between 2% and 12% (Burt et al, 1984; Jagelman, 1987). It seems to develop in a more advanced age group than colo-rectal carcinoma, the average age of manifestation being about 45 years (Sugihara et al, 1982). Periampullary carcinoma is the most frequent cause of death in patients with Gardner's syndrome treated with colectomy and ileo-rectal anastomosis (Jagelman, 1987).

Small bowel polyps result histologically from either lymphoid hyperplasia in the terminal ileum or adenomatous polyps in the ileum and jejenum. They appear to have a low tendency towards malignant change (Burt et al, 1984).

Osteomas of the jaw are one of the originally described features of Gardner's syndrome. They may well occur before the appearance of colonic lesions and are radiologically detectable before becoming clinically apparent. Examination by orthopantomography has therefore been suggested as a useful screening test in children of polyposis coli families (Jagelman, 1987).

References

BURT, R. W., BERENSON, M. M., LEE, R. G., TOLMAN, K. G., FRESTON, J. W. & GARDNER, E. J., 1984. Upper gastrointestinal polyps in Gardner's syndrome. *Gastroenterology*, *86*, 295–301.

GARDNER, E. J. & RICHARDS, R. C., 1953. Multiple cutaneous and subcutaneous lesions occurring simultaneously with hereditary polyposis and osteomatosis. *American Journal of Human Genetics*, *5*, 139–147.

JAGELMAN, D. G., 1987. Extracolonic manifestations of familial polyposis coli. *Cancer, Genetics and Cytogenetics*, *27*, 319–325.

SHEMESH, E. & BAT, L., 1985. A prospective evaluation of upper gastrointestinal tract and periampullary region in patients with Gardner's syndrome. *American Journal of Gastroenterology*, *80*, 825–827.

SUGIHARA, K., MUTO, T., KAMIYA, J., KONISHI, F., SAWADA, T. & MORIOKA, J., 1982. Gardner's syndrome associated with periampullary carcinoma, duodenal and gastric adenomatosis. *Diseases of the Colon and Rectum*, *25*, 767–771.

1990, *The British Journal of Radiology*, *63*, 145–147

Short communications

Cineradiography of a cracking joint

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Human synovial joints are superb bearings which operate on a mixture of boundary and fluid-film lubrication mechanisms. The fluid in the joint, though present in very small amounts, is subjected to a wide range of pressures, from highly positive during loading to negative during rest and parts of the walking cycle. Just as the pressure in the synovial fluid is raised when the joint faces move towards each other, the pressure is lowered as they move apart.

Cavitation is a well documented engineering phenomenon (Knapp et al, 1970) which describes the growth and collapse of gas or vapour bubbles in a liquid. Gaseous cavitation occurs where bubbles grow by gaseous diffusion, for example in carbonated drinks, and is usually harmless. Vapourous cavitation occurs where the local pressure in a liquid drops to its vapour pressure. Bubbles of vapour are then formed, often explosively. This form of cavitation can be extremely noisy and harmful because the vapour bubbles are unstable and collapse violently when a higher ambient pressure is encountered. Fluid machinery such as propellers, pumps and valves are highly susceptible to erosion from this mechanism.

The cracking sound produced by synovial joints has been the subject of scientific curiosity for many years. Roston and Wheeler-Haines (1947) were the first to make a study of the distracting loads needed to produce the sound from the metacarpophalangeal (MCP) joint. Mennel (1947) mentioned that the MCP joint frequently cracked during rigorous examination or therapeutic manipulation. Unsworth et al (1971) conducted an extensive study along similar lines to Roston and Wheeler-Haines (1947), but included investigations of joint geometry, synovial fluid analysis and mathematical modelling. Semlak and Ferguson (1971) concentrated on the physics of the phenomenon *in vitro*, as did Koster (1979). Cracking joints have also been associated with deep-sea divers (Bradley & Vorosmarti, 1974). Joint sounds are also being actively investigated in studies of congenital dislocation of the hip (Cowie et al, 1984) and knee joint pathology (Beverland et al, 1986; McCoy et al, 1987). Watson et al (1989a) conducted an extensive study of the cracking sounds from the MCP joint including long- and short-term variation and the effect of temperature and distraction speed.

Both Roston and Wheeler-Haines (1947) and Unsworth et al (1971) described the appearance of a bubble in the MCP joint space after an antero-posterior radiograph was taken, provided that the joint was kept in tension after cracking. The crescent-shaped shadow that represented the bubble on the radiograph extended to the lateral margins of the joint and made the articular cartilage on the metacarpal head and proximal phalanx base clearly visible. Unsworth et al argued that the cracking sound was produced by the rapid condensation of the vapour phase of this cavitation bubble.

These studies used only static radiographs; however, the mechanism of cracking is dynamic, therefore it was speculated that by using a cineradiograph, more information about the joint movement during cracking and the formation of the bubble could be revealed. Cineradiography has been used extensively in past studies of joints (Saxby, 1970; Ingervall et al, 1971; Weijs, 1975; Fischer et al, 1976; Gernet et al, 1978; Ozaki, 1980; Gonnot et al, 1983; Imamura, 1987; Liu & Sontag, 1987), but only one study (Isberg-Holm & Westesson, 1982) has investigated joint sounds. This sought to link the clicking from the temporomandibular joint with sudden meniscal or facetal movements rather than cavitation.

Method

A 23-year-old healthy male was seated beside the X-ray table so that the palm of his left hand was resting on an empty film cassette. The machine used was a Siemens Seriograph with a 35 mm cine-camera attached. The frame rate used was 120 frames per s which was the maximum available. The beam was aligned so that only the 3rd metacarpal and 3rd proximal phalanx were exposed. Just after the camera was started, the subject was asked to pull his left middle finger until the 3rd MCP joint cracked.

Thirty frames before the crack and 10 frames after were printed at the same magnification on to 5″ × 7″ photographic paper. A frame from the start of the film, when the joint was at rest, was also printed. The distance between the subchondral margins of the bones on the resting frame was measured using vernier calipers. All the subsequent measurements of this distance throughout the sequence were normalized by dividing by the resting measurement.

Results

Three frames pre-crack and one post-crack are shown in Fig. 1. The joint faces have sprung apart between the third and fourth frames and a shadow has appeared in the joint space.

The normalized measurements of the sequence are shown in Fig. 2. There is a slow increase in separation until approximately 0.15 s before the crack. From that point until the crack occurs, the separation appears constant. After the crack, the separation increases rapidly until another plateau level is reached.

Discussion

Normalized measurements taken by 10 individuals from two photographs displayed a variability of 13%, however, since the final measurements were made by one individual, the variability through all the photographs would be considerably less

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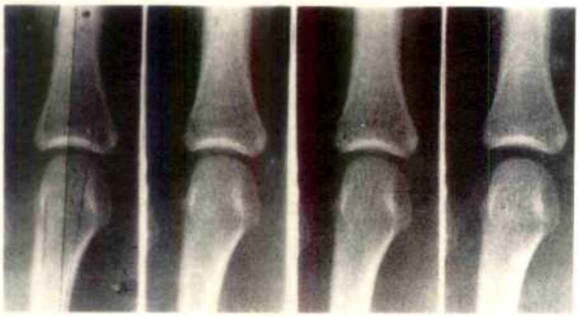

Figure 1. Three frames before and one frame after the MCP joint crack. The frames are separated by approximately 8.3 ms and the bubble has appeared in the joint space between the last two frames.

than this. The quality of the images produced was, of course, reduced because of the size of the film and the short exposure time, therefore the accuracy of measurements is also reduced. However, the effect of this was minimized by the normalization process.

In a previous study (Watson et al, 1989a) the authors demonstrated that the cracking of an MCP joint is a highly repeatable, even characteristic, event for each individual joint. Articular separations were seen to vary with individuals because of differing tissue stiffnesses, so the results presented here are broadly representative, but in absolute terms can only be associated with this one individual.

The results from the film indicated that the bubble was created and was stable between two consecutive frames *i.e.* in less than 8.3 ms. Indeed, its appearance on the radiograph suggests a formation time of much less than this. This would be in agreement with studies of vapour bubble formation (Knapp et al, 1970) under laboratory conditions.

The graph of normalized separations was interesting in two areas:

(1) the plateau before the crack indicated that the soft tissue "slack" had been taken up and the synovial fluid was taking more and more of the load across the joint. The point was reached where it could not support any increase in load, and cavitation occurred, and

(2) after the crack the joint had jumped to almost its maximum separation within two frames (16.6 ms).

The latter result indicated that in future, a more detailed study of this interesting phenomenon will require specialized video or cinematographic equipment to produce frame rates at least 10 times those used here. The study is of value since cracking of the MCP joints has been linked with joint pathology (Watson et al, 1989b). This is a report of a 24-year-old male who cracked his knuckles habitually, up to 25 times a day. He had radiological evidence of chondrocalcinosis and ligamentous ossification.

Experiments to measure the energy released during a crack (Watson et al, 1989a) showed that in some cases a single crack contained enough energy to damage cartilage directly. This has obvious implications with regard to the aetiology of osteoarthritis.

Acknowledgements

The authors would like to thank the staff of the Angiocardiography Department, Belfast City Hospital and the staff of the Withers X-Ray Unit, Musgrave Park Hospital, Belfast for their valuable assistance and advice.

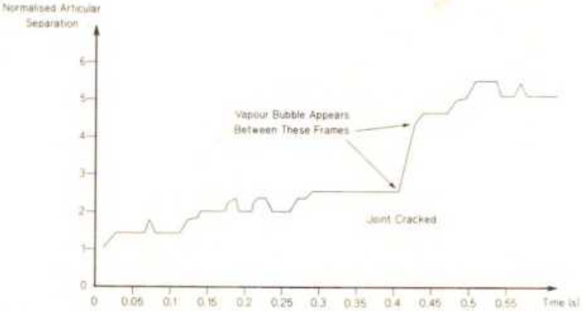

Figure 2. Graph of articular separations normalized to the joint resting separation for 30 frames before the crack and ten frames after.

References

Beverland, D. E., McCoy, G. F., Kernohan, W. G. & Mollan, R. A. B., 1986. What is patello-femoral crepitus? *Journal of Bone and Joint Surgery, 68B*, 496.

Bradley, M. E. & Vorosmarti, J., 1974. Hyperbaric arthralgia during helium-oxygen dives from 100–800 fsw. *Undersea Biomedical Research, 1*, 151–167.

Cowie, G. H., Kernohan, W. G., Bogues, B. A. & Mollan, R. A. B., 1984. Vibration emission in detecting congenital dislocation of the hip. *Orthopaedic Review, XIII*, 73.

Fischer, L. P., Dimnet, J., Gonon, G. P. & Carret, J. P., 1976. Method of the use of X-rays in a cinematic study of joints. Application to the study of the thoraco-lumbar spine in the movement plane of lateral inflexion. *Acta Orthopaedica Belgica, 42*, 125–138.

Gernett, W., Puff, A. & Steinkraus-Maatz, C., 1978. Roentgencinematographic studies on the mechanics of the temporomandibular joint. Function of the temporomandibular joints in patients fitted with full dentures. *Radiologie, 18*, 464–468.

Gonnot, G. P., Mestdagh, H., Deschamps, G., Dimnet, J. & Fischer, L. P., 1983. Cinematic study of the cervical spine during flexion-extension movements. *Bulletin de l'Association des Anatomistes, 67*, 433–443.

Imamura, K., 1987. Cineradiographic study of wrist motion. *Nippon Seikeigeka Gakkai Zasshi, 61*, 499–510.

Ingervall, B., Bratt, C. M., Carlsson, G. E., Helkimo, M. & Lantz, B., 1971. Positions and movements of mandible and hyoid bone during swallowing. A cineradiographic study of swallowing with and without anaesthesia of the temporomandibular joints. *Acta Odontologica Scandinavica, 29*, 549–562.

Isberg-Holm, A. M. & Westesson, P. L., 1982. Movement of disc and condyle in temporomandibular joints with clicking. An arthrographic and cineradiographic study on autopsy specimens. *Acta Odontologica Scandinavica, 40*, 151–164.

Knapp, R. T., Daily, J. W. & Hammitt, F. G., 1970. *Cavitation* (McGraw-Hill, New York).

Koster, D., 1979. Uber einige untersuchungen zur entstehung von gelenkgerauschen. *Beitrage zur Orthopadie und Trumatologie, 26*, 419–427.

Liu, S. Y. & Sontag, K. H., 1987. The guinea-pig step cycle: X-ray cinematographic analysis of the forelimb during pharmacologically induced "stepping automatism". *Experimental Brain Research, 67*, 216–219.

McCoy, G. F., McCrae, J. D., Beverland, D. E., Kernohan, W. G. & Mollan, R. A. B., 1987. Vibration arthrography as a diagnostic aid in diseases of the knee. *Journal of Bone and Joint Surgery, 69B*, 288–293.

Mennel, J., 1947. *The Science and Art of Joint Manipulation* J & A Churchill, London).

Ozaki, J., 1980. Shoulder mechanism—study based on cineradiography and radiography with the arm elevated. *Nippon Seikeigeka Gakkai Zasshi*, *54*, 1679–1692.

Roston, J. B. & Wheeler-Haines, R., 1947. Cracking in the metacarpophalangeal joint. *Journal of Anatomy*, *81*, 65–173.

Saxby, M., 1970. The analysis of cineradiographic records of movements of the temporomandibular joints. *Radiography*, *36*, 170–172.

Semlak, K. & Ferguson, A. B., 1971. Joint stability maintained by atmospheric pressure—an experimental study. *Clinical Orthopaedics and Related Research*, *68*, 294–300.

Unsworth, A., Dowson, D. & Wright, V., 1971. Cracking joints—a bioengineering study of cavitation in the metacarpophalangeal joint. *Annals of the Rheumatic Diseases*, *30*, 348–358.

Watson, P., Kernohan, W. G. & Mollan, R. A. B., 1989a. A study of the cracking sounds from the metacarpophalangeal joint. Proceedings of the Institute of Mechanical Engineers. *Engineering in Medicine*, *203*, 109–118.

Watson, P., Hamilton, A. & Mollan, R. A. B., 1989b. A case of habitual knuckle cracking leading to radiological damage. *British Medical Journal*, Christmas edition (in press).

Weijs, W. A., 1975. Mandibular movements of the albino rat during feeding. *Journal of Morphology*, *145*, 107–124.

A critical appraisal of coagulation studies prior to transfemoral angiography

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The value of requests for coagulation studies prior to angiography is unclear. The rationale that coagulation studies might be helpful in identifying patients likely to suffer from haemorrhagic complications is ill-founded. The primary mechanism of haemostasis following an arterial puncture is the formation of a haemostatic plug, the cellular components of which are the platelets. Aggregation formation on the exposed collagen fibres at the site of puncture results in the formation of a rapid occlusive haemostatic plug (Sixma, 1987). Performing coagulation studies to assess this process is valueless. This can be seen in patients who have haemophilia, where there is a normal bleeding time (a function of the haemostatic plug) but an abnormality of coagulation because of the defects in factor VIII clotting activity.

Previous interest in the coagulation system and angiography has focussed attention on the alteration of coagulation produced by contrast media. *In vivo* and *in vitro* studies with previous higher osmolar agents have suggested that these agents may induce a state of reduced coaguability (Stein & Hilgartner, 1968). Platelet inhibition by contrast media has also been reported, although the newer low osmolar agents have less inhibitory effect (Rao et al, 1985).

In an attempt to refute the need for coagulation studies prior to angiography, we have conducted a retrospective and prospective analysis of haemorrhagic complications in angiography and their relation to coagulation studies.

Patients and methods

Retrospective study

A series of patients having transfemoral arteriography were identified from angiographic records, and the results of laboratory coagulation assays for all patients were obtained. The notes of patients with abnormalities of coagulation were retrieved and any post-procedure complications were noted.

Prospective study

In the 6 month period August 1988–February 1989, 200 consecutive patients admitted for transfemoral angiography were identified from the hospital admissions list. These patients had a full blood count, platelet count and coagulation profile (prothrombin time and thrombin time) performed prior to angiography. During the 24 h following the procedure, these patients were examined for signs of haemorrhage and the need for any intervention was noted.

Survey of practice

A telephone survey of 50 departments of radiology in four Thames regions obtained the practice of that department with respect to angiography and coagulation studies from the senior radiographer in charge of the angiography suite.

Coagulation assays

Platelet counts were performed using a Coulter counter.

Coagulation profiles included the prothrombin time, expressed as the International Normalized Ratio (INR), and the thrombin time. Prothrombin times were performed using the one stage method. The normal range for the INR is 0.9–1.2.

Manual thrombin times were performed, the normal range being 40 s ± 5 s.

Results

Retrospective study

There were 108 patients undergoing arteriography who had coagulation studies available for review. The indications for angiography in these patients were: cardiac, $n = 15$; hepatic, $n = 27$; renal, $n = 10$ and peripheral vascular disease, $n = 56$. Abnormal clotting studies were found in only four cases, and these were in patients undergoing hepatic angiography. Review of the clinical records of these four patients showed that angiography was performed without complication in all these patients.

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Prospective study

Two hundred consecutive angiograms were performed in 6 months. The age range of these patients was 18–86 years with a mean age of 58 years. The indications for angiography were: cardiac investigation, n = 110; cardiac angioplasty, n = 20; hepatic investigation, n = 4 and peripheral vascular disease, n = 66. There were no abnormalities in the full blood counts and platelet counts of these patients. Five patients had abnormal prothrombin ratios; four of these were on therapeutic anticoagulation with warfarin and one patient had known hepatic cirrhosis and abnormal liver function tests. There were no complications in any of the five patients with abnormal coagulation. Minor haemorrhagic complications were seen in 21 patients (10.5%), 13 patients had minor bruising at the puncture site and 8 patients required further pressure haemostasis to the puncture site on return to the ward. No patient required blood transfusion, and there were no major haemorrhagic complications requiring surgical intervention for control of bleeding or evacuation of haematoma. The coagulation studies in these patients were all normal.

Survey results

In the four Thames regions, 50 departments of radiology were contacted; 48 of these centres performed angiography. Of these, 26 (54%) always requested coagulation studies; 18 (38%) never required coagulation studies; one centre (2%) required coagulation studies in patients undergoing angioplasty and three centres (6%) required them for hepatic angiography only.

Discussion

Most studies of the haemorrhagic complications after transfemoral arteriography have confined themselves to the incidence of major bleeding that has required intervention. Hessel (1981) showed that the incidence of haemorrhagic complications requiring treatment and prolonging the patients' stay in hospital was 0.26%.

In a prospective study of angiographic complications, moderate haemorrhage occurred in 3.1% of cases and pronounced haemorrhage in a further 0.9%. Many of these patients were hypertensive and this was cited as an important risk factor (Sigstedt, 1978). After excluding the minor ecchymoses that we recorded, the incidence of haematoma after angiography in our series was 4%. There was no reference in any of these studies to the relationship between coagulation studies and haemorrhagic complications.

The most important observation in our analysis was that patients with abnormal coagulation profiles did not have haemorrhagic complications. To perform these investigations as a screening procedure is also unjustified. The usefulness of pre-operative laboratory investigations has been addressed in a retrospective analysis (Kaplan, 1985). In the analysis of coagulation studies there were only two abnormal results out of the 201 sampled. Both of these were anticipated.

It would appear that requesting coagulation studies prior to angiography is unnecessary as it serves no useful screening function and bears no correlation with haemorrhagic complications caused by angiography. After the control of hypertension, the most important factor in preventing haemorrhagic complications after transfemoral puncture is technique (Herlinger, 1976).

The estimated cost of performing coagulation and platelet studies is £12 per patient. With 700 transfemoral angiographic examinations being performed in this hospital, costs could be reduced by approximately £8000 if, as we would suggest, the policy of requesting routine coagulation studies prior to angiography is abandoned. They should only be performed on patients with a clinically evident bleeding disorder, patients with liver disease and those who are anticoagulated.

Acknowledgments

We are grateful to the surgeons and physicians of King's College Hospital for allowing us to study their patients.

References

HERLINGER, H., 1976. Aortography and peripheral arteriography. In *Complications in Diagnostic Radiology*. Ed. by G. Ansell (Blackwell Scientific, Oxford), pp. 42–75.

HESSEL, S. J., ADAMS, D. F. & ABRAMS, H. L., 1981. Complications of angiography. *Radiology, 138*, 273–281.

KAPLAN, E. B., SHEINER, L. B., BOECKMANN, A. J., ROIZEN, M. F., BEAL, S. L., COHEN, S. N. & NICOLL, D., 1985. The usefulness of preoperative laboratory screening. *Journal of the American Medical Association*, 253, 3576–3581.

RAO, A. K., RAO, V. M., WILLIS, J., BECKETT, C. & STEINER, R. M., 1985. Inhibition of platelet function by contrast media: iopamidol and ioxaglate versus iothalamate. *American Journal of Roentgenology, 156*, 311–313.

SIGSTEDT, B., LUNDERQUIVST, A., 1978. Complications of angiographic examinations. *American Journal of Roentgenology, 130*, 455–460.

SIXMA, J. J., 1987. The role of platelets in haemostasis. In *Haemostasis and Thrombosis*, 2nd edn. Ed. by A. L. Bloom & D. P. Thomas (Churchill Livingstone, Edinburgh), pp. 283–302.

STEIN, H. L. & HILGARTNER, M. W., 1968. Alteration of coagulation mechanism of blood by contrast media. *American Journal of Roentgenology, 104*, 458–463.

1990, *The British Journal of Radiology*, *63*, 149–151

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

Effective dose equivalent in dual X-ray absorptiometry

THE EDITOR—SIR,

The technique of dual photon absorptiometry (DPA) has been established for many years for the measurement of bone mineral density of the lumbar spine and femoral neck. Its use, however, has been mostly restricted to centres with specialized interests. A recent development of the technique has been the replacement of the dual energy isotope source by a dual energy X-ray source. This technique is referred to as dual X-ray absorptiometry (DXA), dual energy X-ray absorptiometry (DEXA) or quantitative digital radiography (QDR). Scanners based on this system are now available from several manufacturers. The use of an X-ray source has resulted in improved image resolution, shorter scan times, better precision (*in vivo* reproducibility of about 1%) and a reduction in radiation exposure per scan. The improved performance of the new machines has led to a wider use of the absorptiometry technique, which is now capable of fulfilling a screening role.

Patients may receive DXA on several occasions in order to establish their rate of bone loss or response to treatment. It is therefore important to be able to reassure such patients about their level of X-ray exposure.

In a review article on bone mineral measurement, Tothill (1989) stated that for DPA "radiation dose is low, around 0.1 mGy to a relatively small volume of tissue. The effective dose equivalent is only a few μSv" but was not more specific. We have measured the entry dose on two commercial DXA machines (Hologic QDR-1000) at two centres, and have also measured a mean dose to the irradiated volume at one centre, with a view to making a realistic estimate of the effective dose equivalent (EDE) associated with spine and femoral neck scans.

The manufacturers of the Hologic QDR-1000 quote an entry dose of 20–50 μSv. At one centre, we obtained a mean entry dose of 35 μSv per scan, based on two thermoluminescent dosimeters each scanned 20 times in spine scan mode. At the second centre, we obtained a mean entry dose of 36.2 ± 2.1 (standard deviation) μSv per scan from 10 measurements using a small energy-compensated GM tube dosimeter (Rad Alert, Perspective Scientific Ltd). All measurements were obtained using anthropomorphic trunk phantoms.

Entry dose, however, is not particularly useful when assessing the total radiation hazard from a particular procedure. Effective dose equivalent is a concept borrowed from occupational exposure estimation and is now commonly applied to estimate doses from nuclear medicine investigations. It represents the total radiation dose to a number of organs weighted according to a risk estimate for each organ concerned (ICRP, 1977).

To estimate the EDE for scans of the lumbar spine, we first estimated the mean dose to the irradiated tissues. The doses measured using the GM tube dosimeter at 0%, 25%, 50%, 75% and 100% depths in a 19 cm thick elliptical hardboard phantom were respectively 36.2 μSv, 35.4 μSv, 23.2 μSv, 12.3 μSv and 6.1 μSv, giving a mean of 22.6 μSv per scan.

Bone, marrow and female gonads are the only named risk organs (ICRP, 1977) in the measurement field. In calculating the EDE we neglected bone and marrow for special treatment because the irradiated masses represent only a small proportion of the total mass of these organs. It is not possible, however, to exclude the female gonads from the calculation because of the variability in their position. For females, the EDE was calculated as follows:

$$\text{EDE} = 22.6 \times \frac{6}{70} \times 0.30 + 23.2 \times 0.25 = 6.4\ \mu\text{Sv}$$

where the mean measured dose has been weighted by the ratio of the mass of tissue irradiated during scanning (6 kg) to the total body mass (70 kg) and also by the weighting factor for "general" tissues (0.30); the gonad dose has been taken as the measured midline dose (23.2 μSv) with 0.25 as the appropriate weighting factor.

For males, the gonads should not appear within the primary beam and so the term in the calculation of EDE relating to the gonads can be dropped, resulting in a value of approximately 0.6 μSv.

For scans of the femoral neck in both males and females, the gonads should not appear in the primary beam and as a similar or slightly smaller tissue volume is scanned the EDE for the male spine is appropriate (*i.e.* 0.6 μSv per scan).

These values of EDE allow us to put the exposure from DXA in context. A modern chest radiograph gives an EDE of about 60 μSv, and the mean daily EDE in the UK to each person from natural sources of radiation is about 5 μSv (NRPB, 1986). Hence, an upper limit to the estimated EDE from a spine scan on a female patient on the QDR-1000 is equivalent to about the daily background if it is assumed that the gonads are in the scanning field. For femoral neck scans on females and males, and spine scans on males, the EDE is only about one tenth of this.

Yours, etc.,

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References

ICRP, 1977. *ICRP Publication 26* (Pergamon Press, Oxford).

NRPB, 1986. *Living with radiation* (Her Majesty's Stationery Office, London).

TOTHILL, P., 1989. Methods of bone mineral measurement. *Physics in Medicine and Biology*, *34*, 543–572.

Changes in relative biological effectiveness with depth of neutron beams

THE EDITOR—SIR,

In his letter on this subject in the August issue of the *British Journal of Radiology* (Hall, 1989), Professor E. J. Hall suggests that "the change of RBE [relative biological effectiveness] with depth is generally *not* seen for high energy neutron beams . . . where the neutron spectrum produced has a single peak". I should like to remind your readers of a study using monoenergetic neutrons from a D–T generator (Nias et al, 1971). We found a 7½% reduction in the RBE value when HeLa cells were irradiated at 10 cm depth compared with those irradiated at the surface.

Yours, etc.,
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(Author's reply)

THE EDITOR—SIR,
(1) The point at issue in my letter (Hall, 1989), and the paper on which it was a comment (Hornsey et al, 1988), was the biological consequences of the difference in neutron spectra characteristic of the reactions involving protons on beryllium versus deuterons on beryllium; 14 MeV D–T neutrons are quite different. They can hardly be regarded as high-energy neutrons, and are nominally monoenergetic except for scattered neutrons from the collimator, and a large γ-ray component.
(2) In reading Professor Nias's reminder that he and his colleagues found a *reduction* in neutron RBE when HeLa cells were irradiated with 14 MeV neutrons at 10 cm depth compared with those irradiated in air, I was intrigued to note that their paper describing this work is entitled "Constancy of biological parameters in a 14 MeV neutron field". This paper concludes that ". . . the neutron therapist can be assured that however much the proportion of primary neutrons, scattered neutrons and γ-radiation may vary at different positions in a 14 MeV monoenergetic neutron beam, variations in the biological parameters are small".

Between writing this paper in 1971 and his present letter in 1989, Professor Nias appears to have changed his mind and now thinks the data show a change of RBE with depth.

On a quick check on the constancy of the neutrons RBE with depth, we have fitted his survival measurements for oxic cells to a linear quadratic form

$$-\ln(S_i) = \alpha_i D + \beta_i D^2$$

where i refers to either in air or at 10 cm depth of water.

Using the standard method of iterative reweighting, our maximum likelihood estimates for α/β are 5.5 ± 3.0 Gy in air and 4.0 ± 2.1 Gy at depth in water. From these numbers, the RBE in air relative to that in water can be estimated, as well as its statistical uncertainty. For example, at 2 Gy (air does), the RBE is 1.2 ± 0.9.

These results would seem to confirm Professor Nias's original statement that "the difference is of doubtful significance".

Yours, etc.,
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References

HALL, E. J., 1989. Changes in relative biological effectiveness with depth of neutron beams. *British Journal of Radiology, 62,* 765.

HORNSEY, S., MYERS, R., PARNELL, C. J., BONNETT, D. E., BLAKE, S. W. & BEWLEY, D. K., 1988. Changes in relative biological effectiveness with depth of the Clatterbridge neutron beam. *British Journal of Radiology, 61,* 1058–1062.

NIAS, A. H. W., GREENE, D. & MAJOR, D., 1971. Constancy of biological parameters in a 14 MeV neutron field. *International Journal of Radiation Biology, 20,* 145–151.

Screening for breast cancer

THE EDITOR—SIR,
It is a pity that in the otherwise excellent review of the UK Breast Screening situation by Professor Forrest he perpetuates two errors of his working party. The first is that a single view is adequate for the initial breast screen. The evidence from Sweden and elsewhere at the time of the publication of the Working Group Report (1979) was quite clearly that the two views were required for the initial screen. The second and more serious error is the recommendation of a 3 year screening interval for which there was, and is, no justification apart from a financial one. To plan propsective studies to prove what is manifestly obvious to every specialist in the field is not only a waste of money and time but is dubious ethically.

Yours etc.,
A. F. MACDONALD

Neuroradiology,
In-patient X-ray Department,
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(Received August 1989)

(Author's reply)

THE EDITOR—SIR,
Dr MacDonald's concern is well known, but it was not one which was shared by his colleagues at the time of the working group's report. Our recommendations for single-view mammography for the basic screen and an interval for screening of 3 years were based on the facts then available. The most recent report of the two-counties study from Sweden is relevant, as it indicates that the 30% reduction in mortality in women invited to be screened by single-view mammography at intervals of 33 months is still maintained at 8 years (Tabar et al, 1989).

Dr MacDonald fails to acknowledge that our recommendations for single-view mammography were "initial" and that the frequency of 3 years was a starting point which should be kept under review. We must know the truth on these matters but this can come only from properly conducted trials, such as those now being set up under the aegis of the UK Coordinating Committee on Cancer Research, and not from the subjective opinions of individual radiologists. To say that prospective well-controlled trials are unethical is but to deny the scientific basis of modern medical practice.

Yours etc.,
P. FORREST

Scottish Cancer Trials Office,
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Medical School,
Teviot Place,
Edinburgh EH8 9AG
(Received October 1989)

References

FORREST, A. P. M., 1989. Screening for breast cancer: the UK scene. The 69th McKenzie Davidson Memorial Lecture. *The British Journal of Radiology, 62*, 695–704.

TABAR, L., FAGERBERG, G., DUFFY, S. W. & DAY, N. E. The Swedish two county trial of mammographic screening for breast cancer: recent results and calculation of benefit. *Journal of Epidemiology and Community Health, 43*, 107–114.

WORKING GROUP, 1979. Report of the working group to review the National Cancer Institute–American Cancer Society Breast Cancer Detection Demonstration Projects. *Journal of the National Cancer Institute, 62*, 639–709.

1990, *The British Journal of Radiology*, *63*, 152–160

Book reviews

Proceedings of the Chest Imaging Conference 1987, Held at the University of Wisconsin-Madison August 31–September 2, 1987. Ed. by W. W. Peppler and A. A. Alter, pp. x + 423, 1988 (Medical Physics Publishing Corporation, Madison, Wisconsin).
ISBN 0-944838-03-0

This publication collects together 45 conference papers, which attempt, in the words of the preface, to be "an update of the present status of radiographic chest imaging". One-third of the papers address what may be considered as conventional technical topics in chest radiology, including a review of radiographic techniques and film–screen technology. The overwhelming emphasis and value of this work is, however, as an update on the emerging research and development work in improving image quality either by optimally modulating exposure of all regions of the chest or by capturing the image on a device with greater latitude than film, or by a combination of both approaches. This is plainly not, nor does it pretend to be, a book about chest imaging in its entirety, and although CT and MRI are briefly discussed there is no mention of nuclear medicine or positron emission tomography (PET).

All of the main research and development topics in the field of chest radiography are covered in the six sections: Film Radiography, Image Processing, Data Storage Transmission and Display, Electronic Detector Systems, Image Perception and lastly Other Topics in Chest Radiography. Most of the papers are clear enough to serve as an introduction to the specific technology being discussed, though a reasonable grasp of basic technical principles is assumed.

Although the main approach is technical, attention is paid to clinical results and at least one-third of the papers are written by radiologists. There are five pairs of papers with one presenting physical performance and the other the corresponding clinical results, some with five years of patient studies.

The need to evaluate diagnostic capability is reflected by the section on image perception, which discusses receiver operating characteristic (ROC) analysis in depth. Some of the introductory discussion of this is rather laboured and could have been better dealt with by reference to a textbook, but the more advanced papers provide an insight into some of the important developments in ROC analysis as applied to multiple abnormalities within an image.

There are ample data presented by most authors, both on technical details and clinical results. The overall impression is that although several of the techniques show promise in enhancing detection of some lesions, particularly in the mediastinal region where the dual effects of poor film latitude and high scatter fractions may be reduced, any overall improvement over traditional techniques has yet to be demonstrated. Indeed, several authors acknowledge how good the standard chest radiograph is in terms or convenience, relative technical ease, low cost and high information content, despite its limitations. The current economic realities are set out in a paper on the financial implications of the new technologies, setting a hard target for these inherently more complex and expensive techniques to meet. Clearly, this is a subject that has passed the first flush of invention and is settling down to the difficult work of improving performance in a very demanding application. The high standard of work reported here gives hope for future success.

The papers are generally well presented, with clear drawings and figures, although the quality of the typeface is variable. The main drawbacks, as with most proceedings, are the lack of an index, little overall editing and the resulting variable quality of content and presentation and a degree of repetition.

This work is a good review of the current status of radiographic techniques, with a firm emphasis on scientific and technical progress. It carries the authority of an author list that includes most of the major workers in the field. Although many of the details have previously been published, the references, reviews and the convenience of a collected work will make this useful to physicists, engineers or radiologists interested in the scientific and technical developments in this field.

A. J. Britten

Essential Radiology in Head Injury: A Diagnostic Atlas of Skull Trauma. By D. Mok and L. Kreel, pp. x + 215, 1988 (Heinemann, London), £35.00.
ISBN 0-433-00041-4

Some 15 years after the clinical introduction of computed tomography in Britain, a large number of conventional radiographs continue to be performed each year for suspected cranial and facial injuries, and there is a diminishing number of doctors competent or confident enough to interpret them. This has caused much wringing or washing of hands according to taste or temperament, but not by the authors of this book: a junior doctor in orthopaedics and an experienced senior radiologist, whose response to this problem has been more constructive. Recognizing the difficulties of young doctors working in Accident and Emergency Departments when they are faced with radiographs of the skull and facial bones, Drs Mok and and Kreel have produced a practical atlas for ready reference when dealing with head injuries.

The authors' stated aims are to encourage a systematic approach to interpretation, provide guidance on when and what additional views may be necessary to make a diagnosis and to illustrate some of the variations of normal and incidental findings that may be encountered. They have managed to do all this in the most admirable fashion in a little over 200 pages, and as only 25 are text, even the most overworked junior doctor should be able to cope before turning to the pictures. There are more than 300 of these, mostly well chosen and good reproductions of plain radiographic appearances and, when necessary, CT images mainly of basal, orbital and facial fractures.

In an introductory chapter of only two pages the authors reiterate the Royal College of Radiologists' selection criteria for skull radiography in the less seriously injured before enumerating those radiological findings in moderate to severe head injuries that are an absolute indication for further investigation and/or admission to a specialist unit. The following eight chapters deal with radiographic projections and normal anatomy, "physiological" intracranial calcification, fractures of the skull and face in adults, skull fractures in children and the normal variants and other appearances that may cause difficulties in interpretation. A short list of references and further reading follows each chapter.

The authors deserve high praise for having dealt with a difficult subject in such a straightforward and unambiguous manner. All the common and important radiological appearances that may be found in cranial and facial injuries are briefly described and, for the most part, well illustrated.

The omissions are minor and perhaps due to brevity. The radiological sign, when present, pathognomonic of a linear fracture, the separation and re-coalescence of the images of the fractures on the outer and inner tables of the skull, are not mentioned. Nor do they say that it is possible to tell the groove made by the middle temporal artery from a fracture of the squamous temporal bone (a problem for both novice and expert) by taking an additional lateral view with a craniocaudal tilt. But these are minor omissions from a thoroughly admirable book which, if readily available, will help to alleviate the present precarious situation in which young doctors find themselves when unsupported by more senior staff. Indeed, it is not only doctors working in Accident and Emergency Departments who would benefit from having ready access to this book; it would also be a valuable bench book for ready reference in departments of radiology. And not just for the registrars.

T. D. HAWKINS

Biomedical Magnetic Resonance Imaging: Principles, Methodology and Applications. Ed. by Felix W. Wehrli, Derek Shaw and J. Bruce Kneeland, pp. xviii + 601, 1988 (VCH Publishers, Germany), £69.00.
ISBN 0–89573–349–8 (USA)
3–527–26701–8 (FDR)

This welcome book is aimed at those seeking greater understanding of magnetic resonance phenomena and technology. An outline format is used throughout, making it a useful and portable reference. Subjects are concisely reviewed, well referenced and explained mathematically when required. There are numerous lucid diagrams and a number of illustrative images. The text is readable and mercifully free from imaginative analogy. Eighteen acknowledged experts and enthusiasts have combined to produce the guide to the how and why of MR.

The bulk of the text (eight chapters) is devoted to the scientific principles of MR with comprehensive coverage of image production and interpretation. The problems of image quality and artefact are addressed at length. There are excellent chapters on flow, magnetopharmaceuticals, multinuclear imaging and high-resolution techniques involving local coils. The biological relaxation of tissues is clearly discussed. This scientific contribution is supported by chapters on biomedical spectroscopy and MR safety.

Imaging of the major organ systems is then reviewed, the emphasis at all times being on technology rather than comparative diagnosis. The book makes no attempt to compete with the MRI texts now available and as such performs a valuable and complementary role. The authors of the clinical sections have a great deal of personal experience with MRI and there is a wealth of practical detail available.

The book is well presented, let down only by the small size of some illustrations, making detail and annotation difficult to read. It should be available in all MR units where I predict it will be widely used as a handbook. Those poised on the interface between imaging and science will find the book especially welcome. Those unfamiliar with MR should, however, read the introductory texts first.

GRAHAM R. CHERRYMAN

Radiological Atlas of Pulmonary Abnormalities in Children, 2nd edn. By Edward B. Singleton, Milton L. Wagner and Robert V. Dutton, pp. viii + 355, 1988 (W. B. Saunders, Philadelphia), £47.00.
ISBN 0–7216–2062–0

As expected of an atlas, the illustrations in this second edition of a *Radiologic Atlas of Pulmonary Abnormalities in Children* are excellent. The authors, all radiologists, present a valuable collection of radiographs unsurpassed by other texts.

Whilst the radiograph still provides the single most important examination of the chest, many other imaging modalities have been illustrated where appropriate. These include xerography, computed tomography, angiography, ultrasound, contrast studies including bronchography and some histology. Very few magnetic resonance images have been included but the authors do state in the preface that in some conditions, this form of imaging will prove of greater value in the future, with improving technology.

In places the layout of the illustrations is poor, with only one or two images per page; this could be condensed, allowing space for further illustrations. However, the quality of reproduction of the illustrations is universally excellent and the legends are concise yet complete and informative; the occasional use of discrete arrows is useful in amplifying the legends.

The page headings are inconsistently present and sometimes inappropriate. For example, illustrations of neonatal goitre, neurenteric cyst and cystic hygroma are all under the page heading of "aspiration of foreign bodies".

Whilst the section on "non-infectious primary pulmonary diseases in the newborn and young infant" is well covered, the text in general is disappointing, adding very little to the legends of the illustrations and, in the case of congenital abnormalities, no attempt is made to elucidate the embryological pathogenesis. The text is occasionally disconcertingly fragmented, ending one page mid-sentence, and continuing for example, nine pages further on. A few surprising omissions are present: instead of some discussion of neurenteric cysts under the appropriate Chapter 4 subheading of "foregut malformations", the reader is referred to Chapter 7 (Pulmonary vascular disease), whilst in fact the only half-line comment on neurenteric cysts is in Chapter 6 under "mediastinal tumours".

At the end of each chapter a bibliography is presented under the appropriate subject subheadings of the chapter. Many of these references are from 1960 or even earlier and could usefully be condensed, particularly when they are not of historical relevance and when more recent references on the same subject are given.

This *Radiologic Atlas of Pulmonary Abnormalities in Children* will be of great value to all radiologists and to clinicians involved in the care of children. The quality and number of illustrations justify the cost of £47 and the book should be included as a reference in all libraries.

CHRISTINE M. HALL

Operative Ultrasound, 2nd edn. Ed. by Bernard Sigel, pp. xii + 219, 1988 (Raven Press, New York), $86.50.
ISBN 0–88167–454–0

There are very few books on operative (otherwise known as intraoperative) ultrasound. This book covers most of the subject well, but it is not really orientated towards radiologists.

The stated aim of the book is "to inform surgeons and their radiologic (sic) colleagues in the use of ultrasound imaging in the operating room". The Editor is Professor of Surgery at the Medical College of Pennsylvania and the contributors are mainly surgeons.

The contents include chapters on instrumentation and techniques as well as one on the basics of ultrasound, an inclusion that seems reasonable in a book aimed at non-radiologists. There are chapters devoted to the use of operative ultrasound in the surgery of various areas of the body and, not surprisingly, these are mainly concerned with the upper gastrointestinal tract (liver, bilary system and pancreas). The use of ultrasound in procedures on the brain and spinal cord and in renal and vascular surgery are also covered.

The print is easy to read and the text well laid out but the contents do constantly remind one of its surgical orientation. I suspect that some of the text was originally written in Japanese and it shows evidence of rather heavy-handed translation. Despite this, it is an easy book to read and it covers most diseases adequately. The illustrations are generally of high quality, although unfortunately too many are produced using old-fashioned bi-stable ultrasound equipment.

The chapter on the liver is comprehensive and also covers some of the newer techniques of liver surgery. This may be useful for those who are not totally up-to-date in this field. The authors take the opportunity to present all their results, which, though interesting, seem out of place.

Equipment sterilization procedures are covered in some detail but only ethylene oxide and the sterile sheath are mentioned. The latter is inconvenient, and in a busy department the former necessitates the purchase of a number of transducers. In the present financial climate this seems inappropriate (transducers cost between £3000 and £7000). I suspect that most British departments will use Cidex for "sterilization" as we do.

One of the important uses of a book of this sort is the provision of a review of the available literature. This book scores well in this area containing numerous references, many of them dated in the recent past (1985–1988).

The final chapter considers the future of operative ultrasound and the thorny question of who should perform the examination. The phrases "close working relationship" and "mutual respect" are much in evidence, but perhaps fortunately no very solid conclusion is reached. This chapter also speculates on the use of operative ultrasound in the surgery of the parathyroid, removal of foreign bodies, the hollow organs of the gut, the breast and the heart.

In conclusion, although this book is heavily biased towards surgery (but this bias should probably also apply to any radiologist who is contemplating getting involved in this work), it covers concisely nearly all of the field. If at times its suggestions seem simplistic to a trained radiologist then it must be remembered to whom it is directed.

I recommend this book to anyone thinking of undertaking this type of work. (It might also be useful reading for registrars who need ideas for papers.) The price of £50 seems a lot for a small book but is in line with most medical publications. If however you are hoping for a well organized life I feel that I should sound one clear warning: **do not let your surgeon read this book**.

GRAHAM PLANT

Medical Imaging: A Concise Textbook. Ed. by Eugene R. Jacobs, pp. xii + 395, 1988 (Igaku-Shoin, New York), £29.75.
ISBN 0–89640–126–X (New York)
4–260–14126–0 (Tokyo)

This paperback has seven contributors, six from the George Washington University Medical Centre in Washington DC. Professor W. L. Olmsted states in his foreword that the book is written for medical students, first-year residents or general medical practitioners "who desire to get a thorough and basic introduction to the specialty of radiology".

The initial chapters discuss the physical processes involved in producing images, radiographic positioning and some aspects of the cost of imaging techniques (with a distinct North American bias). These are followed by a sequence of chapters describing the imaging of body systems. Finally, there is a chapter devoted to the future of imaging in which MRI is mentioned briefly.

Scattered here and there are some classical statements that would be supported by radiologists everywhere, such as "indications for examinations and proper sequencing of examinations must be thoroughly understood and appreciated by the clinician to ensure optimum care" (foreword); "we must abandon the phrase 'ordering an X-ray' and instead consider requesting an 'imaging consultation' " (page 1); "this simple change will lead to more caring examinations tailored to the individual patients' needs with less discomfort, risk, burden and less ultimate cost". Hear, hear! On page 2 there is a lively paragraph on the role of the physician in requesting an imaging consultation — "what information am I seeking?"; "will a positive or negative result. . .alter therapy and. . .outcome".

There is some inconsistency in style. For instance, the chapter on the chest discusses radiological signs and offers some useful "lists". The chapter on the alimentary tract consists largely of illustrative case material, and also discusses radiographic positioning in some (unnecessary) detail (p. 114). Here and there the advice is less than clear — "if you are totally confused by a pulmonary pattern, it is probably an airway pattern" (page 111). Chapters 9–12, on ultrasonography, neuroradiology, interventional radiology and nuclear medicine give good accounts of the usefulness and limitations of these techniques.

Generally, the layout is clear, the illustrations are adequate, there is a good index and most common conditions are mentioned. The book is very good in parts — but who will read it and who will buy it? Medical students may find it expensive, particularly if radiology is not included in the curriculum or in the final examinations. "First year residents and general medical practitioners" are unlikely to appreciate the sections on physics and radiography. Some sections would be useful as a primer for radiological trainees but the book apparently is not intended for this audience. Despite its good points, the book in its present form cannot be recommended to anyone in particular, in Britain at least.

G. M. ROBERTS

Angioscopy: Vascular and Coronary Applications. By G. H. White and R. A. White, pp. xxix + 272, 1989 (Year Book Publishers, Chicago), £56.50.
ISBN 0–8151–9332–7

Have you seen that film about voyaging around the inside of arteries? Angioscopy is like that — but much more difficult, and all that red stuff keeps getting in the way. The movie makers and science fiction writers are usually well ahead of the game, but the scientists are in there battling to catch up, and this book recounts some actions in the battle.

Although the two Whites are given as the authors rather than the editors, they contribute seven chapters to this collection of 24 papers by 38 writers who all work in the United States, except for one cardiac surgeon in Leeds. The chapters cover the history, principles, techniques and uses of angioscopy, together with discussions on the methods of sterilization and equipment available.

The majority of angioscopic investigations have been made following the surgical introduction of the angioscope, and have shown plaque or thrombus in arteries, which has often not been seen on angiograms. It has also been used to see and treat intact valves left in vein grafts, to reduce the size of incisions for *in situ* grafts, and to examine arterial reconstructions. As the instruments have become smaller, percutaneous insertion has become possible, and it has been used to examine lesions treated by dilatation, laser or atherectomy.

This book will be of interest to radiologists and others involved in research into the treatment of arterial disease. Much of the information it gives is scattered through the literature in diverse places, and it will be a considerable help to have it all collected and expanded in this book. For those not so directly involved it may be of interest to look at, but the subject is still too close to the borders of science fiction to threaten angiography — yet.

W. D. JEANS

Imaging in Clinical Practice. By Alan G. Chalmers, James H. McKillop and Philip J. A. Robinson, pp. xii + 340, 1988 (Edward Arnold, London), £16.95.
ISBN 0-340-41214-3

A frequent question that arises during radiological tutorials for membership candidates concerns the choice of a suitable text for the MRCP exam. Until now there has been a limited selection, but this has been extended by the publication of this paperback book. The preface modestly indicates that it is appropriate for membership candidates, but the authors themselves suggest that the book is suitable for preparation for MRCP and FRCS, as well as for older clinicians wishing to update their radiological knowledge. I am sure that it is also a suitable textbook for students preparing for finals and even for first-year FRCR candidates. There are 10 chapters, eight of which cover the major body systems, one on oncology and one on imaging techniques in general. The approach is predominantly problem-orientated with advice as to which imaging technique is likely to be most helpful in a particular clinical situation. There is much useful advice on appropriate use of radiographs and ultrasound and because of the authors' interests, nuclear medicine is well integrated into the text, unlike many other radiological works. There is very little duplication and the book has clearly been well proof-read, although an error has crept into the section on the hazards of radiation. In the assessment of risk from radiological exposure, it is implied that the radiation dose hazard associated with an intravenous urogram (IVU) is equivalent to the risk from smoking 15 cigarettes a day. This could well reduce the demand for IVUs from the clinicians! It is also surprising to see contrast medium referred to as "dye" on a number of occasions.

The quality of the illustrations is extremely high, and this is particularly true of the CT scans, though one or two of the ultrasound images have not reproduced quite as well. Although there is a little discussion of magnetic resonance in the text, there is only one image to illustrate the use of MR and in general it is relegated to being a new technique that may be useful in the future. This is particularly unfortunate in the pituitary where MR now plays an invaluable part in the management of endocrine disorders. There are no direct references in the text but each chapter is accompanied by a brief list of recommended reading.

This book, containing 340 pages and costing only £16.95, is extremely good value for money and should prove suitable for both individual purchase and for incorporation into medical libraries as a guide for examination candidates. Undoubtedly it will prove a fruitful source of questions for future multiple-choice examinations.

JOHN B. BINGHAM

Progress in Digital Angiocardiography. Ed. by P. H. Heintzen and J. H. Bursch, pp. xii + 353, 1988 (Kluwer Academic Publishers, Dordrecht), £80.00; $145.00; Dfl.260.00.
ISBN 0-89838-965-8

It has taken a little time for the research interest in digital imaging techniques for the heart to be accepted into clinical practice. Initially the interest was in intravenous digital subtraction and whether this technique could replace direct coronary and ventricular catheterization. This has proved not to be the case. The focus of interest has now changed to the quantification of angiographic information and data processing. The opportunity that digital imaging gives in the storage and analysis of angiographic data is proving to be a very exciting development area in cardiac diagnosis. One or two books have been published recently dealing with this broad topic; however, this publication is a collection by two of the accepted leaders in the field.

The book is a collection of 30 papers by different investigative groups dealing mainly with the quantification by digital technology of coronary arteriography and left ventriculography. There is a useful introductory chapter by Professor E. Zeitler which discusses the advantages of digital angiography vs NMR as well as setting the scene for the rest of the book. Subsequent chapters deal in depth with particular parameters measured at cardiac catheterization and how digital imaging can be used to measure them. As well as summarizing the present position with regard to quantification of coronary stenoses, measurement of myocardial blood flow, quantification of valve regurgitation and left ventricular function, there are interesting chapters on the future of coronary imaging with discussions on cine computed tomography of the heart and three-dimensional reconstruction of the coronary tree. Most of the book is concerned with adult cardiac disease. As in other books dealing with this subject there is very little discussion on paediatric cardiology except to reinforce the information that digital subtraction enables the reduction of contrast medium dose to the paediatric patient.

Each chapter is concise and, in general, well written with very little repetition of information, despite the multiauthor format. There is heavy emphasis on the presentation of scientific data, many of the chapters taking the form of an extended scientific paper.

The illustrations are of good quality but do not play a prominent role in the book and certainly do not constitute a picture atlas of digital subtraction of the heart.

This is very much a reference book for doctors in the field and as such is certainly to be recommended, although it will have limited appeal to radiologists who are not actively involved in cardiac catheterization. It is expensive for a relatively small book but would be a worthwhile addition to a cardiac-based library. It should also be essential reading to those radiologists who are going to be involved in decision-making on the provision of new cardiac catheterization facilities, since one of the most useful applications of digital technology will be to dispense with the need for 35 mm cine film.

MICHAEL R. REES

Ultrasound: Its Chemical, Physical and Biological Effects. Ed. by Kenneth H. Suslick, pp. xiv + 336, 1988 (VCH Publishers, Veinheim, FRG), DM 138.00; £48.25.
ISBN 0-89573-328-5
3-527-26645-3 (VCH Verlagsgesellschaft

A quarter of a century ago, a classic book with a closely similar title to this, written by the Russian scientist E. L. El'piner, was published in an English translation. Both El'piner's monograph, and this multiauthor volume, have the same objective: to present in a single volume the wide breadth of phenomena and mechanisms resulting from the interaction of ultrasonic waves and the media through which they pass. Thus we find in Suslick's volume separate chapters dealing, for instance, with industrial applications, sonochemistry, acoustic cavitation and sonoluminescence. The two chapters of direct interest for medical users of ultrasound are those by Professor Frizzell and by Dr ter Haar, the latter being the only contribution from outside the USA. In under 40 pages these two chapters summarize well both the biological effects of ultrasound caused specifically by cavitation, and the more general aspects of the possible biological effects of concern in clinical applications. About 150 references are cited in these two chapters alone, enabling reliable access to the main body of literature. Other chapters are likewise excellently referenced, with three each citing more than 200 papers.

A common thread throughout this book is the importance of cavitation as the mechanism of probably the widest importance when considering the effects of ultrasound. Any serious worker studying the interaction of ultrasound and living tissue would find of considerable value the careful discussions by Aldley and Crum on cavitation bubble dynamics, and by Verrall and Sehgal on sonoluminescence. Whilst cavitation is indeed important, I also found Rooney's mature and thorough overview of other non-linear acoustic phenomena of considerable value, including relevant discussions of streaming, cell dispersal and radiation force.

For the clinician who specializes in ultrasound, this book may give valuable insights into the mechanisms underlying present concerns for ultrasound safety. Any scientist studying in detail the interaction of ultrasound with tissue will find this volume to be a long-overdue update of El'piner's monograph, and should be purchased.

F. A. DUCK

Ultrasound of the Prostate. By Matthew Rifkin, pp. x + 293, 1988 (Raven Press, New York), $99.00.
ISBN 0–88167–434–6

Prostate ultrasound is receiving considerable attention from radiologists and urologists on both sides of the Atlantic. Its technology is advancing rapidly, mainly in the field of probe design. It has been variously reported as the definitive test to diagnose and locally stage cancer, a screening modality that will do for prostate cancer what mammography has done for breast tumour, a useful tool for inflammatory disease and, *de rigeur*, the technique required for biopsy. It is increasingly performed by our clinical colleagues, and in fairness to them, it was the clinicians in this country who first started to evaluate the modality seriously. Prostate ultrasound has precipitated many papers but few books. Matt Rifkin's is one of the first.

The first half of the book describes prostate anatomy, embryology, normal ultrasound appearances, scanning and biopsy techniques and reviews the available equipment. Two pages of illustrations are devoted to showing the reader how to place a condom over a probe! On the whole, this is well done, although a little exhaustive. There are plenty of line drawings and the illustrations are of reasonable quality.

Prostate cancer accounts for much of the second half of the book. The staging and grading systems are described, as is the pathogenesis. The various ultrasound appearances of prostate cancer are then tackled. It is this chapter that will attract most attention from readers who want to know whether cancer can be accurately diagnosed and what it looks like. The various appearances are described and well illustrated.

The last part of the book deals with benign and inflammatory prostate and seminal vesical disease. A short chapter on the prostatic urethra describes most urodynamic procedures with a little on ultrasound of the urethra, most of which is of little relevance.

There are likely to be more books on this subject in the pipeline and it is also likely that they will be no better than Matt Rifkin's. There are still many unresolved questions in prostate ultrasound, especially those relating to prostate cancer. Perhaps it's too early for any book on the subject. For those who are interested and already practise prostate ultrasound, this book has little to offer above what is in the current journals. For those embarking on providing a service from scratch, it provides good technical information and introduces the reader to the problems that are still to be solved.

DAVID RICKARDS

Pulmonary Nuclear Medicine. By M. K. Loken, pp. xiv + 396, 1987 (Appleton & Lange, Norwalk, Connecticut), £96.25.
ISBN 0–8385–8070–X

This book is a comprehensive review of all aspects of nuclear medicine involving the lungs. The 19 chapters cover not only the full range of imaging but also the full spectrum of diseases affecting the lungs. Many of the chapters provide both a review of the literature and also a detailed study of a particular, and frequently not well known, aspect of the radionuclides in pulmonary function.

This is a multi-author book (the editor has written three chapters herself) but it reads well with virtually no repetition in the text thanks to good cross-references. The overall editorial standard is also good and the publishers should be complimented on the high quality of the illustrations, which are appropriate.

The book is aimed at physicians, respiratory physiologists and medical students and certainly provides an up-to-date treatise on radionuclide techniques for measurements of lung function, essential for any department that has an interest in pulmonary pathology. I would highly recommend the book to any radiologist who finds chest radiography both a challenge and a stimulus.

I. GORDON

Ultrasound Teaching Cases, Vol. 2. By Keith C. Dewbury, David O. Cosgrove and Hylton B. Meire, pp. ix + 193, 1988 (John Wiley & Sons, Chichester), £45.00.
ISBN 0–471–91681–1

This is a teaching atlas containing 120 ultrasound case studies. There are between 20 and 30 cases under each of the following headings: Liver and Biliary System; General Abdomen; Urinary System; Obstetrics and Gynaecology and a miscellaneous section. The selection of cases is not designed for beginners but for those who already have some experience in diagnostic ultrasound. The conditions illustrated are not particularly rare but the less well known features, unusual presentations and complications of common conditions, *e.g.* a pancreatic pseudocyst presenting as a scrotal swelling! In the less familiar anatomical situations such as breast, the cases are more straightforward. It is not a book designed to teach readers to recognize particular appearances if they encounter them in the future but to illustrate principles that can be incorporated into their own routine practice.

The layout of the book is first class. The relevant clinical details are given first, then the images, followed by a discussion of the findings and finally the diagnosis. The most pleasing aspect of the book is the way in which the images being discussed are always adjacent to the text. The image quality is excellent throughout. It is a reflection of the high image quality that neither line diagrams nor labels are required to explain the images. Each image stands alone and clearly demonstrates the point under discussion. There are many static images, which, although not a true reflection of current practice, is quite acceptable as they are not used at random when a real-time alternative is not available, but quite deliberately when a wide field of view is required, which real-time does not afford. Although I do not agree with the authors' claim that because of its detailed index, the book is, together with Volume 1, a useful reference text, I found it very useful and would strongly recommend it to all those actively engaged in diagnostic ultrasound. It is a book that one can work through with great enjoyment, that one can learn from with surprisingly little effort and that one can come back to without fear of being bored.

M. Gowland

Introductory Medical Statistics, 2nd edn. By R. F. Mould, pp. xii + 192, 1989 (Adam Hilger, Bristol), £9.95.
ISBN 0-85274-382-3

This book is intended primarily for medical science readers such as medical physicists and doctors studying for their FRCR or MCRP. However, it will also prove valuable for a wider group of readers such as biologists, health administrators and, as stated in the preface, any amateur "would-be statistician".

The book explains most of the essential points of medical statistics. Although the earlier chapters are very concise they are easy to follow and a sufficient number of references are listed for every topic explained. The book starts with a chapter on data presentation, and this is followed by a description of curves, distributions and errors, with emphasis on their application in experimental work. Three chapters of the book deal with the theory of probability and explanation of binomial and Poisson probabilities. Additional chapters of the book address and explain the concept of statistical significance. A number of useful statistical tests including χ^2, t, Wilcoxon, and Fisher are outlined. Survival rate calculations and logrank tests are explained in a separate chapter with the aid of worked examples. The final chapter discusses regression analysis.

This book is reasonably priced and it is certainly different from other books available on the subject of elementary medical statistics because of its humour, which I think is an effective way of getting the message across.

Mohi Rezvani

Monte Carlo Simulation in the Radiological Sciences. Ed. by R. L. Morin, pp. viii + 235, 1988 (CRC Press, Florida), £93.50.
ISBN 0-8493-5559-1

Application of Monte Carlo simulation methods to radiological and medical physics problems has become popular in recent years, and this is a timely contribution to the literature on the subject for the learners and investigators in the field.

The book contains seven chapters. The first is devoted to a brief discussion of the elements of probability and statistics with emphasis on binomial and Poisson distributions. The next chapter is concerned with the random number generators (as the fundamental input of the Monte Carlo technique) and tests of randomness and their applications. It would have been constructive to have included a short subroutine demonstrating, for example, a two step generator power residue method for a 32 bit or 64 bit word length.

Monte Carlo simulation of photon transport phenomena, Monte Carlo simulation in diagnostic radiology, nuclear medicine and radiation therapy are the subjects of the remaining chapters of the book.

There are some repetitions from Chapter 4 through to Chapter 7 in the context of the physics of photon transport, but this has been the intention of the authors, and in a way, is interesting and useful for the reader. Although there are no hand computer program examples to tutor the reader through a problem, there are a number of flow charts and numerous references cited.

It is noteworthy that this book has not referred to Monte Carlo simulation at the atomic interaction by interaction level, which is currently a rapidly developing field.

The price of the book is rather high (but then one can say that of most scientific books these days), so it is likely to be a library purchase only. It is a well written book, with good presentation and it would be useful reading for students of physics even if their interest does not lie in Monte Carlo simulation.

Hooshang Nikjoo

Comparative Carcinogenicity of Ionizing Radiation and Chemicals. NCRP Report No. 96. pp. xiii + 179, 1989 (National Council for Radiation Protection and Measurements, Maryland) $16.00.
ISBN 0-913392-96-0

This report reviews the methodologies used to evaluate the carcinogenic risk of radiation with particular reference to their applicability to chemical carcinogens. The mechanisms of action of chemicals are much more varied than ionizing radiation and concepts of "dose" and "dose-response" much less well defined. Add to this the problems posed by *in vivo* metabolism, organ specificity and the associated complexities introduced into mathematical modelling and it is obvious that risk and risk estimate exercises are much more uncertain.

The responsible National Council on Radiation Protection and Measurements (NCRP) Task Group, under the able Chairmanship of Dr A. C. Upton, has sought to summarize cogent evidence from the vast literature on chemical mutagens in order to provide some parallels with radiation effects with which to attempt an assessment of the hazards involved. There are nine major sections and an extensive bibliography. Sections 1 and 2 provide introduction and historical background. Section 3 compares the nature and mechanisms of carcinogenesis as produced by radiations and chemicals. The kinds, distribution and sources of ionizing radiation in the environment are summarized in Section 4 and a similar survey for chemicals is produced in Section 5. Section 6 concentrates on our knowledge of radiation and chemical carcinogenesis in man while Section 7 considers some of the models used to extrapolate to man from experiments with laboratory animals. The very difficult problem of risk assessment is discussed in Section 8 and the volume concludes with a very brief set of conclusions inevitably stressing need for more data.

To attempt such a comparison and survey is a mammoth task, particularly in the light of the enormous range of chemical substances (and their plethora of actions) reported to be carcinogenic, to say nothing of the variations and contradictions which abound in the literature. However, the committee are to be congratulated on producing a very readable, fascinating and, I think, very balanced volume. It makes an excellent introduction to the subject for newcomers and also a timely revision course for those of use who are already in the field.

John R. K. Savage

Problems and Solutions in Radiation Protection. By J. E. Turner, J. S. Bogard, J. B. Hunt and T. A. Rhea, pp. xiv + 301, 1988 (Pergamon Press, New York), £13.50; $24.50.
ISBN 0–08–035552–8

This book is described as consisting of a collection of 74 worked problems in the general field of health protection from ionizing radiation. There could be little that is more revealing of the difference between the work of a health physicist in the nuclear industry and that of a medical physicist in a hospital, or of the difference between the American question and answer style of teaching and the system in the UK, where there are as yet few courses leading to formal qualifications in radiation protection and one is expected to go away and work by oneself, than this collection of 74 worked problems in the general field of protection from ionizing radiation.

As is inevitable in a book of this size which attempts to cover a wide range of subject matter—there are 17 topic headings, ranging from accelerators (two examples) to units—the coverage in each field is sometimes superficial. It is a little surprising to find that in a book which has an excellent section on units, in two of the problems relating to the biological effects of ionizing radiation, there is no mention of SI units, and the problems are worked out in the earlier "special units" for radiation.

In questions relating to external dosimetry, also, the use of the roentgen is perpetuated, which greatly diminishes the value of these worked examples in countries such as the UK where SI units are mandatory. The authors in fact admit that they have not been systematic in this respect along the lines recommended by NCRP Report 82. Also in the section on biological effects, it is surprising that a factor of only 1:2 is used for the effectiveness of fast neutrons relative to that of gamma rays.

With regard to the questions on shielding requirements, care has to be taken in translating the model answers to the UK environment, as the radiation protection criteria employed—for example, a design maximum of 0.5 rem (5 mSv) per year to a member of the public, coupled with the use of occupancy factors—are not applicable in the UK.

However, having pointed out the above shortcomings, this book could be of use as a guide to physicists working in the area of radiation protection, providing care is taken to convert to the appropriate units and design criteria, as there are many relevant examples which could prove useful when confronted with any of a number of practical problems, examples of which are worked through in this book, which is exactly what its title implies—problems and solutions in radiation protection. The average UK medical physicist will encounter about two-thirds of the exmples given in this book, and will find many of them invaluable both as aides-memoire for the methods to be used and as an easy check of the magnitude of the answers to be expected.

Some of the examples will also be of value for general teaching purposes, particularly for Part I of the Fellowship of the Royal College of Radiologists. At £13.50, this book is good value, and a copy should be available in departments of medical physics, particularly for nuclear medicine and radiation protection purposes. A new edition should be produced as soon as possible, using only SI units and embodying the current radiation protection philosophy of the International Commission on Radiological Protection.

Derek Gifford

Cancer Chemotherapy: An Introduction, 3rd edn. By T. J. Priestman, pp. xii + 209, 1989 (Springer-Verlag, Berlin), £19.50.
ISBN 3–540–19551–3 (Berlin)
0–387–19551–3 (New York)

There are now a number of short books on cancer chemotherapy and each sets out with a slightly different purpose. They all have a difficult task in trying to encompass this large, complex and rapidly changing subject in a short space and therefore, as expected, all have their strengths and weaknesses. The third edition of Priestman's book *Cancer Chemotherapy: An Introduction* is a welcome addition to this group of books. It sets out with a very clearly stated purpose: to provide an introductory text rather than a manual. It achieves this purpose very well indeed.

The book is comprehensive and eminently readable. However, it should not be seen as a source of reference for the current management of any particular cancer or the detailed pharmacology of any groups of drugs. It is sufficiently well written to be read right through (perhaps with short breaks!) by someone coming relatively fresh to this field. Its clinical comments are very up to date and accurate. Undoubtedly many specialist oncologists would argue with the occasional point. Perhaps combination chemotherapy does now prolong the survival of patients with multiple myeloma compared to that with single agent chemotherapy, for instance. There is sometimes lack of clarity in dosage recommendations. For instance, mitomycin C cannot be safely given at a weekly dose of 10 mg for long. That is not safe without the most scrupulous supervision of blood counts and it is rarely used this way today.

The section on basic biology is clear and helpful. It gives a little too much emphasis on proliferation dependent cytotoxicity as the basis of the selective effect of cancer chemotherapy. Undoubtedly this plays a part in selective toxicity but the biochemical differences between cells underlie many cases of drug resistance and sensitivity and are probably more important in most cases.

Overall this is a very valuable book that will be useful and cost-effective addition to the shelves of people training in oncology or those who wish to bring themselves up to date with current ideas. It can be thoroughly recommended for this purpose.

P. Selby

Cost Versus Benefit in Cancer Care. Ed. by B. A. Stoll, pp. x + 118, 1988 (Macmillan Press, Basingstoke), £25.00.
ISBN 0–333–43594–X

This short book provides an excellent overview of several different but related problems that face not only cancer physicians, but other groups of doctors too in the whole field of modern medicine.

In his preface, Dr Stoll draws attention to the sensitive area of the limitation of active treatment in advanced disease. Serious ethical problems arise here and the cost of continuing active treatment is not only financial but also relates to the risk of lessening the quality of the remainder of the patient's life rather than improving it. High technology plays its part in this dilemma, as may inappropriate recourse to surgery or intensive cytotoxic chemotherapy. The increasing age of the population in developed countries makes these decisions even more difficult.

In the first section of the book a number of current dilemmas are spelt out and discussed by authors from this country and the United States. The European view is excellently introduced by Dr Stoll himself in considering the concept of overtreatment in cancer, and this is balanced by an American view pointing out among other things that many real and proven advances in cancer treatment have come from an aggressive philosophy and not from conservative approaches. Dr Buzdar's example of a typical M. D. Anderson consent form also bears careful reading. One chapter in this section by Risenhauer and Mackillop from Kingston, Ontario, undertakes a careful discussion on clinical trials.

Two excellent chapters in this first section by Drs Gareth Rees and David Radstone focus on the patient's attitude in Europe, and these are complemented by Dr Brett's commentary on differences of outlook from across the Atlantic. There is a particularly good discussion of the continuing place of paternalism, or at least firm guidance based on knowledge and training, here and elsewhere in this book.

The second part of the book looks at future prospects. There is a most useful discussion on terminal care and dying with dignity, pointing out among other things that at least in the States, hospice care may be no cheaper than conventional methods. From the British side, Drs Ahmedzai and Wilkes write a succinct and useful summary of what hospice care can achieve.

The last three chapters are devoted to aspects of rationing cancer care. Dr Ginzberg points out that despite much talk there has been little evidence of cost containment in cancer care in the United States in recent years. The only retrenchment that can be observed is reduction in access to health care for the poor and uninsured, although fortunately these have not been profound. He feels that the positive orientation of the American public to science and technology are against any retrenchment in this field of medical activity. He does, however, agree that more discussion needs to take place: to form a Policy Agenda on treatment for incurable patients.

The European view by Mooney and Henderson covers some similar issues and asks, pertinently, what value can be proved to arise from the increased expenditure on cancer accorded to American patients as opposed to those in the UK. Quoting a Netherlands source he points out that "if limitation of supply does not result in a decrease of demand, tensions will rise. These tensions may grow to such an extent that under political pressure the demand will have to be met." This has a familiar ring in the recent history of the National Health Service.

In his final chapter, Dr Stoll bravely proposes Guidelines for self-regulation of cost control. These must lead to a balanced relationship between Government and health professionals such that the latter are then prepared to regulate themselves by budgeting, deciding priorities and selecting treatments appropriate for the individual patient. He points out that the amount spent on treating different patients with similar disease often bears no relation to the outcome for the patient (as is now well-known to be the case in other disciplines of medicine too). The six guidelines he goes on to suggest do seem eminently sensible to me, and although such things can never be perfect they do enable the cancer physician to consider difficult priorities in a logical way, which with good fortune should bring greater benefit for the particular patient and for the service as a whole.

Finally, Dr Stoll points out that the consumer representation and self-help groups have an important part to play here. He also suggests the need for an input from a non-political body uninfluenced by Government or by the professions in order to prevent some of the poor decision-making that often arises in the present NHS—such as retention of obsolete hospitals, duplication of expensive technology and ineffective public education on medical issues and choices. He comments that above all, we must reject a purely data-driven approach to treatment which takes little note of either the needs or personal wishes of the individual patient, and that the treatment with the highest response is not necessarily the best buy for the individual.

This is a thought provoking book that all concerned with the care of cancer patients will find interesting. It is well written without serious repetition despite many contributors. It is up to date, and potentially discursive subjects are dealt with crisply, and are to the point. Its general thrust applies not only in cancer, but in the whole field of modern clinical medicine, with the financial, ethical and care issues that confront it, in all countries. Yet it reminds us firmly that in great plans (and reorganizations) the parable of the one sheep lost in the wilderness must not be forgotten.

C. H. Paine

Doppler Ultrasound: Physics, Instrumentation and Clinical Applications. By D. H. Evans, W. N. McDicken, R. Skidmore and J. P. Woodcock, pp. xiv + 297, 1989 (John Wiley & Sons, Chichester), £47.50.
ISBN 0-471-91489-4

The last decade has seen an upsurge of interest in Doppler ultrasound. It is now in widespread clinical use with many new areas of application being demonstrated. There has, for some considerable time, been a need for a comprehensive text on the physical principles underlying the multiplicity of Doppler techniques. Numerous texts are available on the physics of ultrasound and on the clinical applications of Doppler ultrasound, but in both cases the physics of Doppler ultrasound usually receives only cursory coverage.

The stated objective of the book is to provide an up-to-date introduction to the technical aspects of Doppler ultrasound and the authors have successfully achieved this goal. The text has been divided into "essential" and "advanced" reading, the latter being marked by vertical lines in the left-hand margin. There are one or two occasions when essential text contains information whose origin is only apparent if you have read the advanced text, but on the whole the essential/advanced approach works very well and should allow readers from a diversity of backgrounds to make use of the book.

The book is split into 18 chapters of varying length. The first four chapters provide an excellent introduction to the rest of the book covering such topics as the Doppler effect, the theory of flow, basic physics of ultrasound and different types of Doppler system. Chapter 3 on basic physics would have benefited from the inclusion of a simple explanation of the properties of sound waves rather than assuming a certain amount of knowledge on the part of the reader. Nevertheless the chapter was full of useful information such as the effect of the differences in the speed of sound through soft tissue and fat on the apparent position of the sample volume in Duplex systems, or the importance of reflection and refraction on the accuracy of volume flow measurement.

In the central part of the book, Chapters 5 to 11 deal in detail with transducers, Doppler electronics, numerous aspects of signal processing, waveform analysis and volume flow measurement, while quality control and safety are covered in Chapters 12 and 13. All the chapters, with the possible exception of Chapter 8, are well written and lead the reader clearly and steadily through the detailed subject matter. Chapter 8 is entitled "The origin of the Doppler Power Spectrum", and the non-scientist might find even the essential reading rather hard going. For example, the explanation of aliasing, an important concept, appears complicated, and no simple discriptive explanation is given.

The final five chapters give the reader a brief look into the many clinical fields in which Doppler ultrasound has been applied. The clinical examples are introduced in such a way as to illustrate the applications of the physical principles which have been expounded in the earlier chapters.

Overall the book is clearly written, well produced and has very few editorial errors. Cross referencing throughout the book is good and the bibliographies at the end of each chapter are comprehensive and up to date. There are numerous useful line drawings and figures including 33 colour plates. This book is highly recommended and can be considered as essential reading for anyone with a serious interest in Doppler ultrasound.

S. B. SHERRIFF

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Review Article

The development and use of digital subtraction angiography

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The technique of radiographic subtraction was first described in 1935 (Ziedses des Plantes, 1935), although the first English language paper on the subject did not appear until 27 years later (Hanafee & Stout, 1962). This commented that the technique provided an economical photographic method of reducing the confusion of overlapping bony structures in angiographic studies. The advantages of radiographic subtraction can be summarized as (a) providing image enhancement and (b) improving and bringing out detail in areas hidden by overlying bone or poor contrast. These features may therefore save the situation when the density of contrast medium is insufficient to show a lesion (Leeds, 1974). Previously, intravenous injections of contrast medium had been used to show the aorta and other arteries (Steinberg et al, 1959).

Digitization of images was introduced experimentally (Meyers et al, 1963), with the aim of automating the reading of radiographs. Manipulation of digitized information became widely used when computerized tomographic (CT) scanners were introduced, and an early use of computerized subtraction was for the assessment of regional cerebral blood flow (Zilkha et al, 1976) in which pre-injection scans were subtracted from post-injection scans to allow analysis of areas of the scan sections. A series of papers then appeared from workers at the University of Wisconsin describing "computerized fluorography" in which images from an image intensifier were collected, amplified logarithmically and digitized, before being integrated, processed and redisplayed on a monitor (Kruger et al, 1979). The same workers described a "hybrid system" which reduced the storage and amount of digitization of images required (Ergun et al, 1979). Similar work was also being done in the University of Arizona (Ovitt et al, 1980). A comparison of conventional angiography and computerized fluorographic images following intravenous injections of contrast medium was then made, when it was thought that the technique eliminated many of the risks and costs of conventional arteriography (Strother et al, 1980). The name of the technique was modified to "digital video subtraction angiography" (Crummy et al, 1981), and later to "digital angiography" (Mistretta et al, 1981). The name "digital subtraction angiography" (DSA) was first used by a group from the Cleveland Clinic (Meaney et al, 1980), and DSA has become an established abbreviation.

Technical aspects

Types of digital subtraction

Temporal, energy and hybrid subtraction methods have been described.

Temporal subtraction uses a single or an integrated series of images called a mask, as in manual subtraction, which is subtracted from the images containing contrast medium acquired at a different time in the same run. The mask is usually from the start of the run, but may be from the end. As in manual subtraction, movement during image acquisition either by the patient or from respiration, peristalsis of gut, swallowing, cardiac motion or change in calibre of vessels during the cardiac cycle will result in an incomplete subtraction and may cause artefactual changes in the appearance of vessels. Subtraction can be performed using physical variables other than time, such as energy (Riederer & Kruger, 1983).

Energy subtraction has been used in CT scanners, and on an experimental basis in DSA. Pulses of high and low energy X rays are produced, the images digitized and subtracted, producing residual images of the bone and vessels. This is not particularly helpful in displaying vessels without overlying bone, but may be useful in the abdomen, since the pulses are close in time and diminish motion artefacts. There is some increase in skin radiation doses (Foley et al, 1983).

Hybrid subtraction uses energy-subtracted images as a sequence for temporal subtraction and is able to remove both bone images and motion artefacts.

Types of equipment

There are two different types of equipment—the integrated system and the add-on system, each with advantages and disadvantages.

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Integrated systems are produced by the major X-ray equipment manufacturers, and imply a chain of components which have been designed to produce the best images possible. They are more expensive than add-on systems and are either high dose rate continuous or pulsed systems. Both methods are available on some integrated systems, with the pulsed method being preferable since it achieves a high dose rate per image without giving a high dose rate per patient. The high dose rate per pulse means that it is seldom necessary to integrate images by adding several pulses together, and motion artefacts are usually avoided.

Add-on systems take the television signal from a fluoroscopic system and digitize it at 3–25 frames/s. Single images appear granular because of a poor signal-to-noise ratio, and to reduce the noise to acceptable levels several frames are often integrated for both the mask and the subtracted image. Add-on systems are cheaper, and may be mobile, so that if one screening room breaks down they can be moved to another.

Resolution and the components in the chain of equipment

The term resolution relates to both contrast and spatial definition. The contrast resolution of the system is related to its ability to discriminate between the subtracted contrast filled vessel and the "noise" of the system. This noise is produced by quantum mottle, scatter, image intensifier glare, electronic noise and digitization sampling errors. It can be reduced by increasing the dose rate and by averaging the digitized images. Assessment using 0.6–8 mm diameter tubes filled with contrast medium containing 5 mg iodine/ml showed that the minimum diameter of tubes that could be detected varied between 1 and 4 mm for different manufacturers and detection was affected by the radiation dose and the image intensifier diameter used (Busch & Strauss, 1987).

The spatial resolution of photographic film at its maximum is about 10 line pairs (lp) per millimetre, although with medium speed film-screen combinations it is about 4 lp/mm. The theoretical resolution of DSA is limited by the matrix size to 1.28 lp/mm for a 20 cm field using a 512 × 512 matrix. Larger matrices are available, but DSA cannot currently exceed the limitation of about 4.5 lp/mm imposed by the resolution of the image intensifier. The effective resolution is degraded by the presence of movement, which is more apparent in add-on systems than in integrated systems. In early systems, in pulse mode the generator had to make a test exposure before the run (Harrington et al, 1982), but this is now done automatically with control of the iris in the image intensifier to provide the correct light output to the television camera. In continuous mode operation the screening current has to be increased during image acquisition to improve the signal-to-noise ratio, and both this and serial image systems caused reduced X-ray tube life in earlier systems because of the demand for a higher photon flux. Tubes currently being used have a higher rating and usually do not fail prematurely.

The image intensifier and television camera are important links in the chain. The signal-to-noise ratio of all image intensifiers tends to fall fairly rapidly with age, and this will cause a marked reduction in contrast resolution and image quality which may not be apparent unless measurements are made periodically. Larger, 36–40 mm diameter intensifiers are desirable if peripheral angiography is to be done routinely on DSA, but result in reduced spatial resolution. The image processor has a fixed matrix size so that when a larger area is viewed each pixel is larger, giving a reduced spatial resolution in addition to the loss of contrast resolution from increased scatter. This matrix is similar to that of a CT scanner, and its size affects both the spatial resolution and the amount of computer memory required. A matrix size of 512 × 512 contains 262 144 elements of data, each of which contains either 8 bits or 10 bits, and 1 Mbyte can hold about three frames. Twenty-four seconds of imaging at the rate of 25 frames/s required for "cine" type subtraction, or 3 min at the rate of 3 frames/s which is adequate for general vascular work, would produce 600 images, which can be held on a 150 Mbyte disc. One injection for a coronary angiogram uses on average 150 frames, and seven injections are generally made. With a ventriculogram, one patient examination would require about 700 Mbyte of storage (Neeley et al, 1985). If the matrix size were increased to 1 024 × 1 024 the memory required would be quadrupled, and although in theory this should increase spatial resolution, in practice the gain is not as much as expected (Gomes et al, 1986).

The way in which the final image is stored is also a major factor since immediate access to images is limited by storage capacity. Data can be held on digital cassette or as images on video tape, although the latter is only needed for dynamic studies. Selected processed images can be held on permanent discs, or selected images can be put onto film using an image formatter, allowing the original data to be discarded.

A final practical point to consider is the layout of the room and the positioning of the system components. Some computers give off considerable heat and it is inconvenient to have 8 kW of heat produced in an already warm angiographic room on a summer afternoon.

Image manipulation

The major advantage of storage of digital information is that the data can be manipulated to provide more information (Smathers & Brody, 1985), and digital subtraction is only one product of this manipulation.

The contrast level of the image can be altered in the same way that the window level of a CT scanner is altered, and this can be used to enhance the unsubtracted image when subtraction is not applicable.

Movement artefacts can be reduced by "pixel shifting"—changing the position of the mask in relation to the subtracted image to produce the best subtraction.

"Landmarking" can be used to add back into the subtracted image sufficient background detail to allow a surgeon to see the relationship of a vessel to the surrounding bony anatomy.

"Road-mapping" is the ability to present to the angiographer on a television screen the subtracted image with the screening image superimposed to facilitate catheter manipulation. It is occasionally useful, although most angiographers develop a good mental image of the area in which they are operating.

Measurements of width changes or density changes over a time can be made using the data to produce areas, volumes and calculations of percentage stenoses and relative flows. The densitometric method is the more accurate measure of the severity of stenoses since it is reliant neither on spatial resolution nor on assumptions of cross-sectional shape (Key et al, 1987).

Safety aspects

The safety aspects of DSA in comparison with other techniques of investigation are related to radiation doses to patients and staff, the risks of the technique, and the volumes of contrast medium used. The radiation dose to the lens, thyroid, marrow and skin in patients during intravenous DSA done to examine the carotid arteries with a pulsed system was shown to be about 1/20 of that from conventional selective angiography, mainly from the reduction in fluoroscopy time (Pavlicek et al, 1982). In another study the integrated patient dose was about one-third with a median dose of 1 831 R cm^2 for IV-DSA compared with 3 198 R cm^2 for conventional angiography, again mainly because of the reduced fluoroscopy time (Plunkett et al, 1986). Dosage will be higher in continuous fluoroscopic systems than in pulsed systems (Ovitt & Newell, 1985). The dose to staff is also lower when intravenous injections rather than intra-arterial injections are used, because of the diminished screening time, and can be reduced further by using lead glass screens for the face (Britton & Wholey, 1988). However, because intravenous DSA is often regarded as a safer and less invasive examination than conventional angiography, it has been claimed that it can be used more liberally (Carmody & Seeger, 1984) and this would increase the population radiation dose.

The risks of conventional peripheral angiography are relatively low, with complications occurring in 1.7–3% of cases, and deaths occurring in less than one in a thousand patients (Hessel et al, 1981). Risks are greater with transaxillary catheterization, and in centres with fewer cases. Two out of six hundred (0.3%) patients having outpatient transbrachial arterial catheterizations with 4 F catheters for DSA had to have surgery for the complications of haematoma or thrombosis (Gritter et al, 1987). In conventional selective angiography of cerebral vessels for cerebro-vascular disease the risk of stroke is between 0.6 and 5.6% (Leow & Murie, 1988), with an immediate neurological deficit in 11% of patients, the rate being much higher if the examination is done by radiologists in training (McIvor et al, 1987). In a comparative study a 0.8% neurological deficit rate occurred in 780 conventional cerebral angiograms, with a 0.7% rate in 538 intra-arterial (IA) DSA studies done by established neuroradiologists for the investigation of cerebral or carotid disease, whilst no significant complications were seen in 3 710 intravenous (IV) DSA examinations (Stevens et al, 1989). It seems clear that the procedural risks of IV-DSA are negligible compared with the risks of intra-arterial injections either selectively or into the arch in the investigation of cerebro-vascular disease.

The dosage of contrast medium can become very large with repeated injections, and one death (thought to have been due to ventricular asystole) is known to the author to have occurred in a patient who received 300 ml non-ionic contrast medium (350 mg I_2/ml) intravenously during the investigation of disease at multiple sites. It is prudent to keep a running tally of the volume of contrast medium used and keep within a maximum dose of 300 ml contrast medium or 4 ml/kg using 300 mg I_2/ml.

Techniques of injection

Intravenous injections can be given peripherally or centrally. In experiments using repeated injections into the cephalic vein, the subclavian vein and the main pulmonary artery in a dog, more central injections caused a greater density in the femoral artery over a shorter time (Rubin et al, 1984). There was little improvement with pulmonary artery compared with superior vena cava (SVC) injections, and it is thought that pulmonary artery injections with ionic contrast medium increase the central volume and reduce the cardiac output.

Peripheral intravenous injections can be made through a 16 G butterfly needle or preferably through a short intravenous catheter placed in the basilic vein on the medial side of the arm; 30–50 ml of contrast medium containing 300–370 mg I_2/ml are injected at a rate of 15 ml/s, and this is repeated for each view or position.

The advantages of peripheral intravenous examinations are that they are quicker since they can be done without using sterile packs, the short intravenous catheter can be put in place outside the catheter room and no arterial compression is required after the procedure. Patients having both central and peripheral injections of ionic contrast media prefer the peripheral ones (Popky et al, 1984). Comparisons of images produced after peripheral and central injections in the same patients showed no significant difference in image quality in one study (Lea Thomas & Treweeke, 1986), but most angiographers prefer to use central injections in the belief that these produce better images. Central intravenous injections are made through a pigtail catheter positioned in the superior vena cava or right atrium, using the standard exchange technique. The volume of contrast medium is the same as for peripheral injections, but the rate can be increased to 25 ml/s. Injections into the right atrium produce mixing with blood from both the IVC and the SVC, giving a uniformly opacified bolus (Saddekni et al, 1985).

It was found soon after the introduction of DSA that intravenous injections are of little use in patients with poor cardiac outputs, in those who are breathless, or those who cannot keep still, and the use of non-selective arterial injections was then advocated (Crummy et al, 1982).

Non-selective arterial injections can be made following brachial or femoral catheterization, and 4 F or 5 F gauge catheters can be used, although the flow rate through 4 F catheters may be too slow to get optimum opacification. The catheter can be positioned in the ascending aorta for injections to show the extracerebral vessels, or in the abdominal aorta to show abdominal and peripheral vessels. The volumes and density of contrast medium will be smaller than for intravenous injections, with a total iodine load greater than that used in conventional angiography. If the image intensifier available will not allow both legs to be shown in the conventional position, the patient's legs can be crossed just before injection to show both legs down to the ankle, but separate injections will be needed to show each foot (Gersten et al, 1986).

Selective arterial catheterization allows the use of less dense contrast medium in smaller volumes than for conventional angiography, and the immediate availability of subtracted or unsubtracted images on the television screen for study speeds investigations and makes interventional angiographic procedures considerably easier.

Improvements in image quality can be made by various means. Bright spots should be reduced by good coning and the use of lead rubber strips around the area of interest. In the neck, bolus bags of the type previously used for CT examinations can be used to reduce glare. Patients should be rehearsed in holding their breath and not swallowing before the injection is made. In the abdomen, injections of Buscopan or glucagon can be used to reduce peristalsis. Peripheral vasodilatation is needed to examine the small arteries of the hands, and this can be improved by warming the limb or by rebreathing into a bag to increase carbon dioxide concentrations.

Clinical applications

Cerebral and extracerebral vascular disease

The commonest use of DSA has been in the investigation of extracerebral vascular disease. Peripheral intravenous injections were found to demonstrate the carotid arteries as well as central intravenous injections, but intracerebral vessels were shown better with central injections (Modic et al, 1983). The satisfactory demonstration of the carotid bifurcation using intravenous injections has varied in different studies from 26% (Hoffman et al, 1984) to 93% (Wood et al, 1983) of examinations, with superimposition of vessels, poor opacification, patient movement and swallowing all contributing to poor quality, together with the poor opacification found in patients with poor cardiac output. Intravenous DSA is generally agreed not to have had the success initially hoped for (Cebul & Paulus, 1986). Up to five injections are necessary, and even then some lesions may be missed since it has been shown that lesions are seen in one view only in 44% of patients having three views of each bifurcation at selective angiography (Jeans et al, 1986). Intra-arterial DSA with injections in the ascending aorta gives better images and can be done on outpatients (McCreary et al, 1985), but carries a higher risk to the patient. The apparent "safety" of IV-DSA has led to a less vigorous assessment of the need for a contrast medium examination, with risk of a consequent increase in population exposure to radiation (Leow & Murie, 1988). With conventional angiography before the widespread use of Doppler, 7.4 angiograms were done for each carotid endarterectomy performed (UK–TIA Study Group, 1983). The figure must be very much higher for centres using intravenous DSA as a "screening" procedure, and figures for the 'replacement value' or percentage of IV-DSA investigations needing no further evaluation by other techniques (Health Technology Case Study 34, 1985) should be treated with caution since techniques avoiding radiation are preferable for screening purposes when appropriate. Doppler ultrasound is now well established as a screening method for carotid bifurcation disease (Lusby et al, 1981) and its comparison with DSA and angiography has shown that the bifurcation can be seen more often with Doppler than DSA, suggesting that Doppler should be the primary screening technique (Glover et al, 1984; Mendel et al, 1987). It has also been recommended for the follow-up of patients after endarterectomy (Zbornikova et al, 1986). It is our practice to use Doppler to screen the carotid arteries in patients with transient ischaemic attacks or bruits, and to do intra-arterial DSA only in those patients in whom there is difficulty in interpreting the Doppler studies.

Intracerebral examinations can be done using intravenous injections in specific problems such as the exclusion of an unsuspected aneurysm in patients with parasellar masses shown on computed tomography, looking for the presence of arterio-venous malformations, in the investigation of tinnitus or the follow-up of aneurysms after surgery (Carmody & Seeger, 1984), but the method is not recommended for looking at intracerebral atheroma (Ernest et al, 1983). The simultaneous opacification of all the cranial vessels makes it difficult to define the separate feeding vessels to tumours or lesions requiring angiography before treatment and these are best examined by selective angiography. Digital subtraction angiography can be used to carry out the examination faster. The decision to record the lesion on standard film or on DSA will depend on the spatial resolution required to demonstrate the abnormality completely.

Pulmonary angiography

Patients with suspected emboli have been examined with IV-DSA, and a recent trial comparing peripheral injections with conventional angiography found that DSA was useful for showing emboli in the central pulmonary vessels, but both false negative and false positive diagnoses were made in smaller vessels in the peripheral third of the lung because of overlap of vessels, and poor image quality from cardiac and respiratory movement (Musset et al, 1988). In the UK a greater reliance is placed on the results from clinical assessment combined with chest radiographs and pulmonary perfusion and ventilation scans, so that there is less demand for pulmonary angiography than in some other countries.

Cardiac imaging

Digital subtraction has been mainly applied in three areas—the assessment of left ventricular function, the examination of the coronary arteries, and during coronary angioplasty. Left ventricular function may need to be assessed after myocardial infarction, particularly when aneurysm formation is suspected and when peripheral embolism has occurred, during assessment of coronary artery disease before and after operation, and in cardiomyopathy (Wholey, 1985). Segmental wall movement can be assessed satisfactorily by DSA (Foster et al, 1988), and the ability to calculate measurements of left ventricular function (Mancini & Higgins, 1985) and arterial stenoses from the digital data could prove valuable in making decisions on the need to operate and in surgical audit. There are few areas of diagnostic imaging which have the combination of requirements of high spatial, temporal and contrast resolution needed in coronary arteriography (Neeley et al, 1985). The ability to combine early and late images has been used to demonstrate the length of occluded segments of coronary artery prior to dilatation (Carlson et al, 1987). Replacement of routine cine angiography with IA-DSA and selective catheterization is possible, but is still hampered by the need for very large memory capability to hold more than a few patients' examinations, and the difficulty of long-term storage of recall of examinations (Neeley et al, 1985). This is changing as digital cassette storage becomes available. In congenital heart disease DSA can provide information that is nearly equivalent to film or cine methods (Tonkin, 1985), but the rapid development of echocardiography, colour flow Doppler and magnetic resonance may reduce the usefulness of both DSA and conventional angiography in assessment of ventricular function and congenital abnormalities.

Abdomen and kidneys

Both intravenous and intra-arterial injections have been used in this area. In the liver a comparison of intra-arterial DSA with conventional angiography showed that small vessels were not so well seen, but changes in the parenchymal phase were easier to see (Flannigan et al, 1983). The technique is also useful for assessing the portal system, and the integration of early arterial and late portal and mesenteric vein images may be useful to the surgeon.

Intravenous DSA has been advocated for screening hypertensive patients for renal artery stenosis (Smith et al, 1982), although both false negative and false positive cases were found. A later study has also shown that 10% of examinations were uninterpretable or incorrect on IV-DSA (Wilms et al, 1986). In examining potential donors for renal transplants, small accessory renal arteries may be missed (Rabe et al, 1983). Screening of hypertensive patients for renal artery abnormalities is culturally and speciality dependent. Many physicians feel that in older patients hypotensive therapy is now so effective and the results of dilating atherosclerotic arteries so variable that there is no point in screening such patients. All younger patients should be screened, and isotope renography can demonstrate those kidneys with a reduced renal blood flow. In such patients intra-arterial angiography should be done so that dilatation can be performed at the same session if a suitable lesion is found. The definition of 'younger' will vary from place to place, but should certainly apply to anyone under 45.

Aortography and peripheral vessels

In all patients with symptoms of peripheral disease a clinical and physiological assessment with exercise testing and Doppler ankle pressure measurements should be done to decide if angiography is required, and there is no place for angiographic "screening".

As with all DSA investigations an injection of contrast medium is needed to show each site, so that four to five injections will be required to look at the distal aorta and peripheral vessels, the volume being increased when the intravenous route is used (Kaufman et al, 1984). In aorto-iliac occlusive disease, intravenous injections can be used to show the origin of the occlusion and the distal reconstituted arteries. In the majority of patients no other investigation is needed (Rosen et al, 1983). Similar results have been found in non-specific aorto-arteritis or Takayasu's disease (Sharma et al, 1989). Peripheral vessels may not be well shown, and the quality can be improved by integration of a series of images (Lewis et al, 1984). The ability to do post-processing image manipulation to improve the quality of information available is one of the major advantages of DSA.

A prospective trial of peripheral angiography using conventional films, DSA and a combination of the two showed that DSA alone was unsatisfactory but that it had a useful complementary role in resolving problems, and that its use reduced film and contrast medium costs (Garvey et al, 1986). In addition to these savings there is said to be a 12% overall reduction in costs when capital costs are included (Norman et al, 1985). We have found that intra-arterial injections into the femoral artery using a 22 G needle provide a quick and simple way of showing vessels down to the feet when these are not demonstrated by conventional means, or when the state of the aorto-iliac segment is not in question. In trauma affecting the extremities, a comparison of intravenous and conventional angiography showed that both techniques had an equal diagnostic ability, with DSA being quicker, more convenient and more economic (Sibbitt et al, 1986). Intravenous studies provide a method of assessing the results of surgery if other methods of assessment are not available (Teeuwen et al, 1989).

Selective and other studies

In selective arteriography and in interventional angiographic procedures such as angioplasty and embolization, DSA speeds up procedures by providing an immediate image which may be subtracted or not, according to need (Chang et al, 1984). This is an undoubted benefit, and there is a saving on film costs since only selected images need be produced as a final record.

The technique is also useful in looking for changes in contrast medium density that are difficult to see in conditions such as carotico-cavernous fistulae (Modic et al, 1982), in the diagnosis of venous leakage in the corpora cavernosa in impotence following cavernosography (Hartnell et al, 1988) and in laryngography when air provides a satisfactory contrast medium (Brown et al, 1983).

Conclusions

Before the introduction of DSA the trend in arteriography was towards increasing selectivity of catheterization for specific problems with the aim of improving visualization of the vessel or target organ, and the avoidance of overlying and confusing vascular opacification. In addition there was a search for improved spatial resolution, particularly in coronary angiography. Intravenous DSA tried to reverse these trends, but has proved to be acceptable in limited situations only—when looking for gross lesions in relatively large arteries of the size of the carotid upwards, when arterial access is difficult, and in some post-operative investigations.

The principal benefits of DSA are those that were defined for radiographic subtraction, with the addition of immediacy, and they are most obvious in association with intra-arterial injections where the high density of contrast medium over a short period produces clear images (Dawson, 1988). Contrast medium loads are reduced, procedures carried out more rapidly, film costs reduced, and the use of small-diameter catheters allows diagnostic examinations to be done on outpatients.

Digital subtraction angiography cannot be considered separately from other methods of investigation. Doppler ultrasound is effective in screening for the presence of disease in the carotid vessels, is increasingly useful in congenital and valvular disease of the heart, and is the primary method of assessment of peripheral vascular disease. Radionuclide perfusion and ventilation scans are satisfactory tests for pulmonary embolism in most patients, and angiography is needed only if massive embolization is thought to have occurred. Computed tomography is effective in diagnosing aortic dissection, and both CT and ultrasound show the overall size and the intraluminal haematoma within aneurysms better than any arteriographic method.

The optimum DSA systems are the intregrated type produced by a single manufacturer and these will be justified in centres with a high angiography load, such as those with a dedicated vascular, cardio-vascular or neurosurgical service. Acceptable images can be produced using add-on units, and these will meet the needs of less intensive users until the prices of the larger systems fall, their memories are increased and the long-term storage and immediate recall of digital images comes closer to realization.

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References

Britton, C. A. & Wholey, M. H., 1988. Radiation exposure of personnel during digital subtraction angiography. *Cardiovascular and Interventional Radiology, 11*, 108–110.

Brown, B. M., Enzmann, D. R., Hopp, M. L. & Castellino, R. A., 1983. Digital subtraction laryngography. *Radiology, 147*, 655–657.

Busch, H. P. & Strauss, L. G., 1987. Comparison of performance characteristics of different DSA-installations. *European Journal of Radiology, 7*, 56–59.

Carmody, R. F. & Seeger, J. F., 1984. Intracranial applications of digital subtraction angiography. *CRC Critical Reviews in Diagnostic Imaging, 23*, 1–40.

Carlson, E. B., Morris, K. G., Hinohara, T. & Sinetos, A. L., 1987. Digital subtraction angiography in angioplasty of total coronary artery occlusion. *Chest, 92*, 560–562.

Cebul, R. D. & Paulus, R. A., 1986. The failure of intravenous digital subtraction in replacing carotid angiography. *Annals of Internal Medicine, 104*, 572–574.

Chang, R., Kaufman, S. L., Kadir, S., Mitchell, S. E. & White, R. I., 1984. Digital subtraction angiography in interventional radiology. *American Journal of Roentgenology, 142*, 363–366.

Crummy, A. B., Strother, C. M., Lieberman, R. P., Stieghurst, M. F., Sackett, J. F., Wojtowycz, M. M., Kruger, R. A., Turnipseed, W. D., Ergun, D. L., Shaw, C. G., Mistretta, C. A. & Ruzicka, F. F., 1981. Digital video subtraction for evaluation of peripheral vascular disease. *Radiology, 141*, 33–37.

Crummy, A. B., Stieghurst, M. F., Turski, P. A., Strother, C. A., Lieberman, R. P., Sackett, J. F., Turnipseed, W. D., Detmer, D. E. & Mistretta, C. A., 1982. Digital subtraction angiography: current status and use of intra-arterial injection. *Radiology, 145*, 303–307.

Dawson, P. 1988. Digital subtraction angiography—a critical analysis. *Clinical Radiology, 39*, 474–477.

Ergun, D. L., Mistretta, C. A., Kruger, R. A., Riederer, S. J., Shaw, C. G. & Carbone, D. P., 1979. A hybrid computerised fluoroscopy technique for noninvasive cardiovascular imaging. *Radiology, 132*, 739–742.

Ernest, F., Houser, O. W., Forbes, G. S., Kispert, D. B., Folger, W. N. & Sundt, T. M., 1983. The accuracy and limitations of intravenous digital subtraction angiography in the evaluation of atherosclerotic cerebro-vascular disease: angiographic and surgical correlation. *Mayo Clinic Proceedings, 58*, 735–746.

Flannigan, B. D., Gomes, A. S., Stambuk, E. C., Lois, J. F. & Pais, S. O., 1983. Intra-arterial digital subtraction angiography: comparison with conventional hepatic arteriography. *Radiology, 148*, 17–21.

Foley, W. D., Keyes, G. S., Smith, D. F., Belanger, B., Sieb, L. E., Lawson, T. L., Thorsen, M. K., & Stewart, E. T.,

1983. Work in progress: temporal energy hybrid subtraction in intravenous digital subtraction angiography. *Radiology*, *148*, 265–271.

Foster, C. J., Butler, P. & Freer, C. E. L., 1988. Digital subtraction of the left ventricle. *British Journal of Radiology*, *61*, 1009–1013.

Garvey, C. J., Wilkins, R. A. & Lewis, J. D., 1986. Peripheral vascular disease: prospective study of intraarterial digital subtraction angiography using a 9 inch intensifier. *Radiology*, *159*, 423–427.

Gersten, K., Pillari, G., Greenspan, B., Rosen, E. & Zito, J., 1986. Crossed-leg technique for digital subtraction angiography. *American Journal of Roentgenology*, *146*, 843–844.

Glover, J. L., Bendick, P. J., Jackson, V. P., Becker, G. J., Dilley, R. G. & Holden, R. W., 1984. Duplex ultrasonography, digital subtraction angiography and conventional angiography in assessing carotid atherosclerosis. *Archives of Surgery*, *119*, 664–669.

Gomes, A. S., Papin, P. J., Mankovich, N. J. & Lois, J. F., 1986. Digital subtraction angiography: a comparison of 512^2 and 1024^2 imaging. *American Journal of Roentgenology*, *146*, 835–838.

Gritter, K. J., Laidlaw, W. W. & Peterson, N. T., 1987. Complications of outpatient transbrachial intraarterial digital subtraction angiography. *Radiology*, *162*, 125–127.

Hanafee, W. & Stout, P., 1962. Subtraction technic. *Radiology*, *79*, 658–661.

Harrington, D. P., Boxt, L. M. & Murray, P. D., 1982. Digital subtraction angiography: overview of technical principles. *American Journal of Roentgenology*, *139*, 781–786.

Hartnell, G. G., Mulcahy, M. J., Kiely, E. A., Williams, G. & Allison, D. J., 1988. Digital subtraction dynamic cavernosography. *British Journal of Radiology*, *61*, 679–682.

Health Technology Case Study No. 34, 1985. The cost-effectiveness of digital subtraction angiography in the diagnosis of cerebrovascular disease (Office of Technology Assessment, Washington, DC).

Hessel, S. J., Adams, D. F. & Abrams, H. L., 1981. Complications of angiography. *Radiology*, *138*, 273–281.

Hoffman, M. G., Gomes, A. S.& Pais, S. O., 1984. Limitations in the interpretation of intravenous carotid digital subtraction angiography. *American Journal of Roentgenology*, *142*, 261–264.

Jeans, W. D., Mackenzie, S. & Baird, R. N., 1986. Angiography in transient cerebral ischaemia using 3 views of the carotid bifurcation. *British Journal of Radiology*, *59*, 135–142.

Kaufman, S. L., Chang, R., Kadir, S., Mitchell, S. E. & White, R. I., 1984. Intraarterial digital subtraction angiography in diagnostic arteriography. *Radiology*, *151*, 323–327.

Key, H., Jackson, P. C., Thomas, E. A., Jeans, W. D. & Davies, E. R., 1987. The accuracy of digital subtraction angiography for the quantification of atherosclerosis. *British Journal of Radiology*, *60*, 1083–1088.

Kruger, R. A., Mistretta, C. A., Houk, T. L., Riederer, S. J., Shaw, C. G., Goodsitt, M. M., Crummy, A. B., Zwiebel, W., Lancaster, J. C., Rowe, G. G. & Flemming, D., 1979. Computerised fluroscopy in real time for noninvasive visualisation of the cardiovascular system—preliminary studies. *Radiology*, *130*, 49–57.

Lea Thomas, M. & Treweeke, P. S., 1986. Intravenous digital subtraction angiography: a comparison of peripheral versus central contrast injection. *British Journal of Radiology*, *59*, 241–244.

Leeds, N. E., 1974. Image enhancement with magnification and subtraction. *Radiologic Clinics of North America*, *12*, 241–256.

Leow, K. & Murie, J. A., 1988. Cerebral angiography for cerebrovascular disease: the risks. *British Journal of Surgery*, *75*, 428–430.

Lewis, B. D., Enzmann, D. F., Guthaner, D. F. & Brody, W. R., 1984. A high frame rate digital subtraction angiography imaging technique for evaluation of aorto-femoral run-off. *Radiology*, *151*, 789–790.

Lusby, R. J., Woodcock, J. P., Skidmore, R., Jeans, W. D., Hope, D. T. & Baird, R. N., 1981. Carotid artery disease: a prospective evaluation of pulsed Doppler imaging. *Ultrasound in Medicine and Biology*, *7*, 365–370.

Mancini, G. B. J. & Higgins, C. B., 1985. Digital subtraction angiography: a review of cardiac applications. *Progress in Cardiovascular Diseases*, *18*, 111–141.

McCreary, J. A., Schellhas, K. P., Brant-Zawadski, M., Norman, D. & Newton, T. H., 1985. Outpatient DSA in cerebrovascular disease using transbrachial arch injections. *American Journal of Roentgenology*, *145*, 941–947.

McIvor, J., Steiner, T. J., Perkins, G. D., Greenhalgh, R. M. & Clifford Rose, F., 1987. Neurological morbidity of arch and carotid arteriography in cerebrovascular disease. The influence of contrast medium and radiologist. *British Journal of Radiology*, *60*, 117–127.

Meaney, T. F., Weinstein, M. A., Buonocore, E., Pavlicek, W., Borkowski, G. P., Gallagher, J. H., Sufka, B. & MacIntyre, W. J., 1980. Digital subtraction angiography of the human cardiovascular system. *American Journal of Roentgenology*, *135*, 1153–1160.

Mendel, H. J., Olbert, F., Schlegl, A. & Nebosis, M., 1987. Duplex ultrasonography, intravenous digital subtraction angiography, intraarterial digital subtraction angiography and conventional angiography in assessing carotid atherosclerosis. *Annales de Radiologie*, *30*, 115–120.

Meyers, P. H., Becker, H. C., Sweeney, J. W., Nice, C. M. & Nettleton, W. J., 1963. Evaluation of a computer-retrieved radiographic image. *Radiology*, *81*, 201–206.

Mistretta, C. A., Crummy, A. B. & Strother, C. M., 1981. Digital angiography: a perspective. *Radiology*, *139*, 273–276.

Modic, M. T., Berlin, A. J. & Weinstein, M. A., 1982. The use of digital subtraction angiography in the evaluation of carotid cavernous fistulas. *Ophthalmology*, *89*, 441–444.

Modic, M. T., Weinstein, M. A., Pavlicek, W., Gallagher, J., Duchesneau, P. M., Buonocore, E. & Meaney, T. F., 1983. Intravenous digital subtraction angiography: peripheral versus central injection of contrast material. *Radiology*, *147*, 711–715.

Musset, D., Rosso, J., Petitpretz, P., Girard, P., Havvy, M. P., Simonneau, G., Labrune, M. & Duroux, P., 1988. Acute pulmonary embolism: diagnostic value of digital subtraction angiography. *Radiology*, *166*, 455–459.

Neeley, J. P. III, Vannier, M. W., Gutierrez, F. R. & Spadaro, J. J., 1985. Digital subtraction angiography of the coronary arteries. *CRC Critical Reviews in Diagnostic Imaging*, *25*, 23–60.

Norman, D., Ulloa, H., Brant-Zawadzki, M. & Gould, R. G., 1985. Intra-arterial digital subtraction imaging cost considerations. *Radiology*, *156*, 33–35.

Ovitt, T. W., Christenson, P. C., Fisher, H. D., Frost, M. M., Nudelman, S., Roehrig, H. & Seeley, G., 1980. Intravenous angiography using digital video subtraction: X-ray imaging system. *American Journal of Roentgenology*, *135*, 1141–1144.

Ovitt, T. W. & Newell, J. D. II, 1985. Digital subtraction angiography: technology, equipment and techniques. *Radiologic Clinics of North America*, *23*, 177–184.

PAVLICEK, W., WEINSTEIN, M. A., MODIC, M. T., BUONOCORE, E. & DUCHESNEAU, P. M., 1982. Patient doses during digital subtraction angiography of the carotid arteries: comparison with conventional angiography. *Radiology, 148,* 265–271.

PLUNKETT, M. B., GRAY, J. E. & KISPERT, D. B., 1986. Radiation exposure from conventional and digital subtraction angiography of cerebral vessels. *American Journal of Neuroradiology, 7,* 665–668.

POPKY, G. L., SALUK, P. H., GRISKA, L B., PARKER, J. A. & CONSIGNY, P. M., 1984. Comparison of superior vena cava and antecubital vein as DSA injection site. *American Journal of Roentgenology, 143,* 317–319.

RABE, F. E., SMITH, E. J., YUNE, H. Y., KLATTE, E. C., LEAPMAN, S. B. & FILO, R. S., 1983. Limitations of digital subtraction angiography in evaluating potential renal donors. *American Journal of Roentgenology, 141,* 91–93.

RIEDERER, S. J. & KRUGER, R. A., 1983. Intravenous digital subtraction: a summary of recent developments. *Radiology, 147,* 633–638.

ROSEN, R. J., ROVEN, S. J., TAYLOR, R. F., IMPARATO, A. M. & RILES, T. S., 1983. Evaluation of aorto-iliac occlusive disease by intravenous digital subtraction angiography. *Radiology, 148,* 7–8.

RUBIN, D. L., BURBANK, F. H., BRADLEY, B. R., & BRODY, W. R., 1984. An experimental evaluation of central versus peripheral injection for intravenous digital subtraction angiography. *Investigative Radiology, 19,* 30–35.

SADDEKNI, S., SOS, T. A., SRUR, M. & COHN, D. J., 1985. Contrast administration and techniques of digital subtraction angiography performance. *Radiologic Clinics of North America, 23,* 275–291.

SHARMA, S., AGGARWAL, S., TALWAR, K. K. & RAJANI, M., 1989. Intravenous digital subtraction angiography in non-specific aorto-arteritis. *British Journal of Radiology, 62,* 117–120.

SIBBITT, R. R., PALMAZ, J. C., GARCIA, F. & REUTER, S. R., 1986. Trauma of the extremities: prospective comparison of digital and conventional angiography. *Radiology, 160,* 179–182.

SMATHERS, R. L. & BRODY, W. R., 1985. Digital radiography: current and future trends. *British Journal of Radiology, 58,* 285–307.

SMITH, C. W., WINFIELD, A. C., PRICE, R. R., HARDING, D. R., TUCKER, S. W., WITT, W. S. & HOLLIFIELD, J. W., 1982. Evaluation of digital venous angiography for the diagnosis of renovascular hypertension. *Radiology, 144,* 51–54.

STEINBERG, I., FINBY, N. & EVANS, J. A., 1959. A safe and practical intravenous method for abdominal aortography, peripheral arteriography and cerbral angiography. *American Journal of Roentgenology, 82,* 758–772.

STEVENS, J. M., BARTER, S., KERSLAKE, R., SCHNEIDAU, A., BARBER, C. & THOMAS, D. J., 1989. Relative safety of intravenous digital subtraction angiography over other methods of carotid angiography and impact on clinical management of cerebrovascular disease. *British Journal of Radiology, 62,* 813–816.

STROTHER, C. M., SACKETT, J. F., CRUMMY, A. B., LILLEAS, F. G., ZWIEBEL, W. J., TURNIPSEED, W. D., JAVID, M., MISTRETTA, C. A., KRUGER, R. A., ERGUN, D. L. & SHAW, C. G., 1980. Clinical applications of computerised fluoroscopy. The extracranial carotid arteries. *Radiology, 136,* 781–783.

TEEUWEN, C., EIKELBOOM, B. C. & LUDWIG, J. W., 1989. Clinically unsuspected complications of arterial surgery shown by post-operative digital subtraction angiography. *British Journal of Radiology, 62,* 13–19.

TONKIN, I. L. D., 1985. Digital subtraction angiography in congenital heart disease. *Seminars in Roentgenology, 20,* 283–289.

UK-TIA STUDY GROUP, 1983. Variation in the use of angiography and carotid endarterectomy by neurologists in the UK-TIA aspirin trial. *British Medical Journal, 286,* 514–517.

WHOLEY, M. H., 1985. Cardiovascular applications of digital subtraction angiography. *Radiologic Clinics of North America, 23,* 627–639.

WILMS, G. E., BAERT, A. L., STAESSEN, J. A. & AMERY, A. K., 1986. Renal artery stenosis: evaluation with intravenous digital subtraction angiography. *Radiology, 160,* 713–715.

WOOD, G. W., LUKIN, R. R., TOMSICK, T. A. & CHAMBERS, A. A., 1983. Digital subtraction angiography with intravenous injection: assessment of 1000 carotid bifurcations. *American Journal of Roentgenology, 140,* 855–859.

ZBORNIKOVA, V., ELFSTROM, J., LASSVIK, C., JOHANSSON, I., OLSSON, J.-E. & BJORNLERT, U., 1986. Restenosis and occlusion after carotid surgery assessed by duplex scanning and digital subtraction angiography. *Stroke, 17,* 1137–1142.

ZIEDSES DES PLANTES, B. G., 1935. Subtraktion. Eine röntgenographische Methode zur separaten Abbildung bestimmter Teile des Objekts. *Fortschritte auf dem Gebiete der Röntgenstrahlung, 52,* 69–79.

ZILKHA, E., LADURNER, G., ILIFF, L. D., DU BOULAY, G. H. & MARSHALL, J., 1976. Computer subtraction in regional cerebral blood volume measurements using the EMI scanner. *British Journal of Radiology, 49,* 330–334.

1990, *The British Journal of Radiology*, *63*, 169–180

Final Report of the general clinical results of the British Institute of Radiology fractionation study of 3F/wk *versus* 5F/wk in radiotherapy of carcinoma of the laryngo-pharynx*

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Abstract. The 10 year follow-up of a clinical trial involving the comparison of 3F/wk *versus* 5F/wk in radiotherapy of squamous cell carcinoma of the larynx and hypopharynx has now been completed. The trial involved an intake of 734 patients between 1966 and 1975. The classification of all patients has been revised to conform with the latest TNM publication. A reduction in total dose was made for 3F/wk compared with 5F/wk. This varied between 13% and 11% in centres treating over 3 weeks and 6 weeks, respectively. No statistically significant differences have been found between the two arms (3F/wk *versus* 5F/wk) of the trial in any of the main group analyses. A number of sub-group analyses relating to survival, tumour-free and laryngectomy-free rates and to the comparison of acute or late normal-tissue radiation damage have also been performed. No differences have been found that could be considered to be statistically significant in relation to the particular sub-group. Previous interim reports suggested minor differences in sub-group analyses between the 3F/wk and 5F/wk regimes in this trial; these have diminished now that the full follow-up data are available. This trial has provided evidence on which clinicians may base their choice between either a 3F/wk fractionation regime or a conventional 5F/wk treatment protocol in the treatment of carcinoma of the laryngo-pharynx.

During his Presidential year, 1962–1963, Dr Frank Ellis called together clinicians, physicists, radiobiologists and statisticians, at the British Institute of Radiology, to consider a multidisciplinary research project into time/dose relationships in clinical radiotherapy. After wide-ranging discussions a Working Party was formed with Dr Ellis as its first Chairman. They published a Preliminary Report (1963) which summarized the then relevant and important issues, concentrating particularly on the problems associated with achieving a scientifically and statistically valid result when testing a hypothesis in the field of clinical practice. Many clinical trials had foundered, and regrettably still do, for lack of an adequate number of patients being available and because of the poor design of the trial without enough provision for follow-up. Few useful retrospective analyses of clinical data were available (Fleming & Wiernik, 1963). Details of the Working Party's solutions to these questions were published in the First and Second Progress Reports (1964, 1968). The agreed clinical trial for treatment of squamous carcinoma of larynx and hypopharynx was to break new ground not only in the scientific questions it addressed but in being, possibly, the first solid tumour cancer therapy study in the UK that was multicentre, thus recruiting relatively large numbers of patients with comparatively uncommon cancers. The trial was prospective, randomized and utilized a "null-hypothesis" basis through which it was intended to produce no significant difference in the reactions of normal tissues between the 3F/wk and the 5F/wk groups, thereby making it possible, on ethical grounds, to complete the study.

Some preliminary results were published (Third Progress Report, 1970), with suitable provisos concerning the limitations associated with such interim

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Patients were entered into the trial from the following centres: Bristol (J. Bullimore, S. Curwen, R. C. Tudway); Coventry (K. Sicher); Exeter (R. C. M. Hadden); Glasgow (T. B. Brewin, R. S. Bundi, J. C. Davidson, G. E. Flatman, T. Habeshaw, K. E. Halnan, F. Kelly, F. McGurk, E. H. Porter, H. Yosef); Liverpool (M. A. Stewart); London: Charing Cross Hospital (D. O'Connell, N. Howard), London Hospital (W. Shanks), Middlesex Hospital (N. M. Bleehen, Sir Brian Windeyer), Royal Free Hospital (D. Skeggs), St Thomas' Hospital (T. D. Bates, I. F. J. Churchill-Davidson); Newcastle (R. Finney, W. M. Ross); Oxford (K. R. Durrant, F. Ellis, A. H. Laing, C. H. Pain, G. Wiernik); Plymouth (J. M. Brindle); Reading (J. S. Bunting); Southend (D. L. Phillips); Stoke-on-Trent (R. Lindup, D. Meredith-Brown, E. R. Monypenny); Swansea (D. K. Sambrook).

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data, which were made available so as to give reassurance both to all participants and to the many observers of this pioneering multicentre venture.

The best estimates suggested that there was no imbalance between the two arms of the trial. Hand-sorted data were reported for survival, acute normal-tissue reactions, tumour recurrence and the incidence of laryngectomy. A similar up-date of short-term results was published in the Fourth Progress Report (1971). For the first time, this included a list of patients who had been entered into the trial but who, for stated reasons, were considered unsuitable for analysis and were, therefore, withdrawn.

By 1972 (Fifth Progress Report), the collected data had been entered into a computer and the first actuarial survival rates had become available. It was reported that a review of the histological slides for patients entered into the trial was to be undertaken so as to ensure that no undetected bias should influence the conclusions to be drawn from the results. A review was achieved and it confirmed that there was an equal distribution of well-differentiated and poorly differentiated carcinomata in both arms of the trial. In only one patient was the diagnosis of malignancy not confirmed at this review, although one other patient had already been withdrawn from the trial, for a similar reason: the centre which had entered this patient had started treatment prior to the histological confirmation of the clinical diagnosis (Seventh Interim Progress Report, 1982).

In the Sixth and Seventh Interim Progress Reports (1978, 1982) the changing patterns of observed survival rates, recurrence-free and laryngectomy-free rates, as well as in those of late normal-tissue reactions, were discussed. It was pointed out that caution was needed in the interpretation of such incomplete data as the variations that apparently appeared could be due to a variety of possible causes, some of which were explored in more detail (Wiernik, 1980, 1981).

In all these interim reports it was stressed that the most reliable conclusions that could be drawn from this trial had to await the availability of all the late follow-up data. This final report on the BIR fractionation trial is based on data that are now available after a 10 year follow-up has been completed on all patients. The report is being published in several parts. The present paper presents the general clinical results and other data will be submitted for publication in appropriate journals. Three abstracts based on oral presentations of different aspects of the data from the final analysis have already been published (Wiernik & Rezvani, 1988, 1989; Rezvani et al, 1989).

Materials and methods

To obtain a fuller understanding of the planning, execution and updating of this successful multicentre, prospective, randomized clinical trial of treatment of squamous cell carcinoma of the larynx and hypopharynx, reference should be made to the Preliminary and the subsequent seven Interim Progress Reports (1963, 1964, 1968, 1970, 1971, 1972, 1978, 1982). The protocol for entry of patients into this trial required that randomly allocated treatment schedules be used, either three fractions per week (3F/wk), given with a minimum interval of 48 h between fractions, or five fractions per week (5F/wk). The same overall treatment time had to be used for both schedules, with no planned gap in treatment. In each participating centre the length of the course of treatment was a matter of choice, being based on their standard practice. A reduction in the total radiation dose was employed for treatments with 3F/wk compared with 5F/wk. This reduction was 11–13% for overall treatment times of 6–3 weeks, respectively.

For this Final Report the entire computer data-file, which was added to regularly as fresh follow-up data became available, was fully checked against the follow-up forms. Entry to the trial was terminated at the end of 1975, by which time the number of patients entered was 734 with a mean age of 62.7 years in each of the two treatment arms.

Twenty-one patients have been omitted from this study and Table I gives the details. From this table it can be seen that there were four cases that had been listed as excluded previously (Fifth, Sixth and Seventh Reports, 1972, 1978, 1982); there were six new exclusions and 11 cases that had been excluded previously under the heading of patients for whom full data had not yet become available. These 11 patients represented the total number of cases entered by one centre that used a "split-course" which incorporated a planned gap in the middle of the treatment. It was considered that these various exclusions would not affect the validity of the randomization procedure. Five patients previously excluded because of variations in treatment from the

Table I. Patients allocated prospective random numbers but excluded from all analyses

Trial number	F/wk	Reason for exclusion
12017	3	Had tuberculosis. Radiation treatment stopped.
14020	5	Records say "cancelled" and no other correspondence.
14039	3	Histology not malignant.
15002	5	Records say "cancelled".
15013	3	Metastases in lung seen after entry.
21073	3	Lung metastases seen after start of treatment.
24011	3	Withdrawn. Wrong diagnosis.
24021	3	Wrong diagnosis—carcinoma of tongue.
24053	3	No folder. Card says died of coronary before treatment commenced.
24060	3	Entered trial in error. It was his second treatment.
Centre 13	3 and 5	11 patients treated by split-dose regimes.

allocated regime have been re-entered as it is now considered that the variations in their methods of treatment did not amount to a violation of the treatment protocol. Therefore there are now 713 patients included in the final analyses.

In the 24 years that have elapsed since the entry of the first patient into this trial, the separate brochures listing the TNM classification of malignant tumours by the International Union against Cancer have been collected together into the Livre de Poche (UICC, 1968). This has been revised four times. Fortunately, the detailed design of the forms used for entry of patients into this trial had allowed the classification of all patients according to the latest TNM edition (UICC, 1987) for their T status (extent of primary tumour). However, because the whole basis for the N classification (regional lymph node metastasis) has changed in the 4th Edition (UICC, 1987), and now requires the actual nodal dimensions, for which no records are available, the 3rd Edition (UICC, 1978) has been used for the N classification of the patients being analysed. The trial protocol excluded all patients with positive distant metastases (M). The stage grouping (S) for larynx and hypopharynx for T and N, when M is zero, is similar in the 3rd Edition and the 4th Edition of UICC (1978, 1987) and so it has been considered acceptable to allocate the patients in this trial to a stage grouping (S) despite the hybrid nature of the T and N components. Detailed considerations concerning the application of the TNM system to the data available in this trial are too extensive for inclusion in the present report and will be published elsewhere (Wiernik et al, 1990). For the larynx classification there were sufficient data to allow patient allocation into each of the T categories T1, T2 and T3. However, for the pharynx classification the original data sheets did not carry the information concerning tumour fixation which is now required for allocation into categories T3 and T4 and so patients with possible T2, T3 and T4 lesions have had to be included in the pharynx category T2. Thus the analyses presented do not differentiate between pharynx T2, T3 and T4 categories.

The classification of patients into the two sub-groups, "cords mobile" and "other sites" (Sixth Interim Progess Report, 1978), which was forced upon us by the previous lack of adequate computer facilities, has now been overcome and all data have been classified according to the TNM system (UICC, 1978, 1987). The previous cords mobile sub-group corresponds only with the current T1 category as it does not take N (regional lymph node metastases) into consideration. However, in clinical practice the S (stage grouping) classification is far more realistic as prognosis depends so heavily on the nodal status (Johns et al, 1984). When the glottic T1 tumours were assessed for their nodal status, out of a total of 288 patients only five had positive nodes and so there is very little difference between the old sub-group cords mobile and the present sub-group S1. However, it was felt necessary to include the old cords mobile method of analysis in this Final Report, to present up-to-date data for comparison with the previously published Interim Reports. This was essential in order to be able to demonstrate clearly that any diminished difference between the 3F/wk and the 5F/wk groups was due to the full follow-up data that are now available rather than leaving doubt as to whether the change was attributable to the new method of analysis.

The patients who had tumours involving only laryngeal subsites were distinguished from those who had tumours confined to pharyngeal subsites by allocation to separate sub-groups that were analysed according to the larynx or pharynx classifications, respectively. The patients who had tumours extending to anatomical subsites classified by the TNM system (UICC, 1987) under both larynx and hypopharynx were grouped, for the present analysis, under a separate sub-grouping named "dual tumours". All patients falling into the larynx T4 category, which by definition involves pharyngeal structures, have been included in the dual tumours sub-group. For technical reasons, the larynx T categories were used for the classification of all patients in the dual tumours sub-grouping. The patients who had tumours confined to the aryepiglottic fold, who could have been classified as either primary laryngeal or pharyngeal tumours, were classified as dual tumours. For the purpose of analysis, the pharynx and dual tumour sub-groups were combined, since a review of the data, according to the anatomical site, had shown that the survival of patients in these two subsites was similar and different from the survival of patients with tumours in the larynx subsite. The survival of patients with aryepiglottic fold tumours was closer to that of patients with pharyngeal and dual tumours than to the survival of patients with laryngeal tumours, a finding that is similar to previous reports (Lederman, 1970).

Distribution of the patients in the three groups listed above and in the two treatment arms is shown in Table II. Although none of the differences between the two arms is significant at the 5% level, there are higher proportions of S1 patients and larynx patients in the 3F/wk group. Any effect that this might have on the comparison of treatment results between the two groups has been taken account of by multivariate analyses using Cox's proportional hazards model (Cox, 1972).

All analyses that appear in this report, unless otherwise stated, are based on raw data. Although provision was made on the original data sheets for full information concerning the cause of death, we have, in the majority of patients, received inadequate information concerning post-mortem examinations when a patient died from an intercurrent illness and, so as not to run the risk of biasing our results, we have had to attribute all deaths to cancer.

Detailed considerations of the radiobiological data (Rezvani et al, 1989, 1990), the inter-relationship of ear, nose and throat surgery with radical irradiation (Alcock et al, 1990), data relevant to clinical trials (Haybittle et al, 1990) and the physical/dosimetric comparisons which were carried out in association with the National Physical Laboratory (Barrett et al, 1990) will be published elsewhere.

Table II. Distribution of number of patients in the 3F/wk and 5F/wk treatment groups according to TNM classification

	TNM classification												
	T1		T2+T3+T4		N0		N1+N2+N3		S1		S2+S3+S4		Total
Fractions per week	3	5	3	5	3	5	3	5	3	5	3	5	
Larynx	175	148	93	104	258	243	10	9	171	143	97	109	520
Pharynx	12	21	6	10	9	16	9	15	5	10	13	21	49
Dual tumours	2	5	63	74	38	47	27	32	2	5	63	74	144
Total	189	174	162	188	305	306	46	56	178	158	173	204	713

Results

Tumour responses

Observed survival rates

The observed crude survival rates for patients treated with 3F/wk and 5F/wk are shown in Fig. 1a. All patients entered into the trial have been included except for the 21 exclusions listed in Table I. Initially the survival rates are shown at 3 monthly time intervals, then, between 2 and 5 years, at 6 monthly and later at yearly time intervals. The number of patients at risk, entering each time period, are shown across the top of the panel. The χ^2 and the corresponding p values, shown on the graph, refer to the comparison of the survival rates over the two periods 0–5 years and 0–10 years, respectively. The error bars shown at these time points represent the 95% confidence limits for the probability of survival. The χ^2 values were obtained from the comparison of the survival data using the method of Mantel (1966). It can be seen that there is no significant difference between the two treatment groups. A multivariate analysis including age, sex, site, stage, T, N and treatment group showed that only age, stage and site were significant independent prognostic factors, mortality being higher in older patients, more advanced stages and patients with pharyngeal or dual tumours. With these three factors included, the relative risk for the treatment effect (*i.e.* ratio of mortality rate in the 3F/wk arm to that in the 5F/wk arm) was 1.05 with a 95% confidence interval of 0.87–1.27. Thus the relative risk was apparently marginally in favour of 5F/wk. This was in contrast to the survival curves calculated without taking into account the imbalance of prognostic factors where the 3F/wk group appeared to have a slight advantage. However, the differences were not statistically significant ($p=0.60$ and 0.44, respectively).

A similar comparison was made using the entire data, including the 21 excluded patients listed in Table I. This is not illustrated but it made little difference to the survival data shown in Fig. 1a except for slightly changing the values of χ^2 to 0.77 ($p=0.38$) at 5 years and χ^2 to 0.62 ($p=0.43$) at 10 years. When an age correction for natural mortality is applied to the raw data (Fig. 1b), it can be seen that it does not influence the comparison between 3F/wk and 5F/wk although, of course, the relative survival rate at 10 years was raised by approximately 21%.

A sub-group analysis of all patients in the S1 stage grouping (T1N0) is shown in Fig. 2a; there was no significant difference in survival whether they were treated with 3F/wk or with 5F/wk. This is true for the remainder of the patients, when those in S2, S3 and S4 stage groupings were combined (Fig. 2b). There was a statistically significant difference ($\chi^2=85.57$, $p<0.0001$)

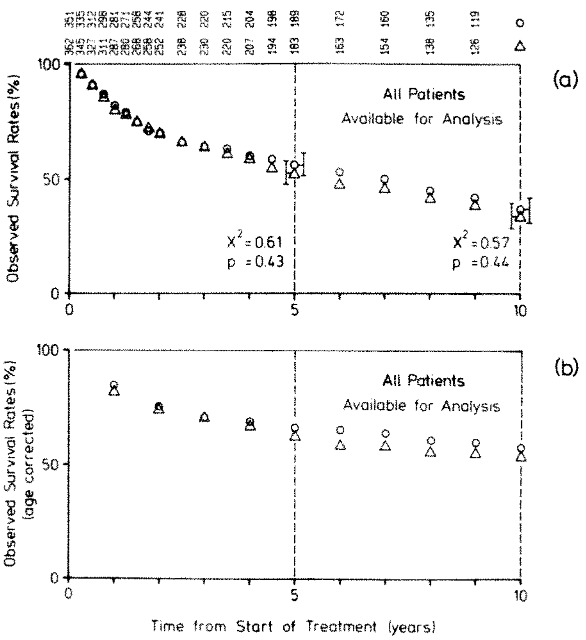

Figure 1. (a) Observed (*i.e.* crude) survival rates of all patients entered into the trial, with the exception of the 21 patients listed in Table I, *versus* time from start of radiation treatment. No correction for age of the patients or mortality of patients without cancer is made. The values of χ^2 are obtained by the method described by Mantel (1966); $p<0.05$ would normally indicate a statistically significant difference when all data are included in the analysis but for sub-groups $p<0.025$ may not even be safely assumed to be statistically significant. (b) shows a representation of the above data "age-corrected". The numbers of patients surviving at the beginning of each time point are shown across the top of the panel (○, 3F/wk; △, 5F/wk).

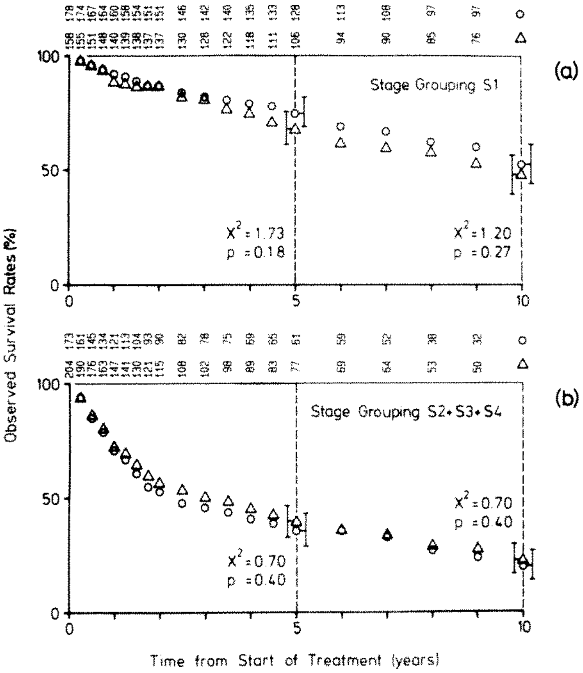

Figure 2. Observed survival rates as in Fig. 1a but confined to patients (a) in the S1 stage grouping and (b) in the S2, S3 and S4 stage grouping. Symbols as in Fig. 1.

Table III. Percentage survival tumour-free and laryngectomy-free rates related to type of treatment and site of primary tumour

	Larynx		Pharynx and dual tumours	
	3F/wk (268)[a]	5F/wk (252)[a]	3F/wk (83)[a]	5F/wk (110)[a]
Survival rates ±SE (%)				
at 3 years	74±3	76±3	32±5	37±5
at 5 years	66±3	66±3	25±5	28±4
at 10 years	42±3	44±3	20±4	12±3
	$\chi^2 = 0.01$, $p = 0.92$		$\chi^2 = 0.01$, $p = 0.92$	
Tumour-free rates ±SE (%)				
at 3 years	64±3	66±3	35±6	31±5
at 5 years	62±3	65±3	32±6	26±5
at 10 years	57±3	63±3	32±6	26±5
	$\chi^2 = 1.43$, $p = 0.23$		$\chi^2 = 0.08$, $p = 0.78$	
Laryngectomy-free rates ±SE (%)				
at 3 years	76±3	83±3	82±5	67±5
at 5 years	74±3	82±3	82±5	65±6
at 10 years	70±3	82±3	82±5	65±6
	$\chi^2 = 5.93$, $p = 0.01$		$\chi^2 = 4.74$, $p = 0.03$	

Statistics refer to the comparison of rates for 3F/wk *versus* 5F/wk from entry into the trial to 10 years after treatment.
[a] Numbers in parentheses are the numbers of patients at entry.

between the S1 stage grouping and the S2, S3 and S4 stage groupings, and survival was higher in the S1 stage grouping. Separate comparisons of 3F/wk with 5F/wk treatments in larynx sites and in pharynx plus dual tumour sites (Table III) showed no significant differences between the two treatment regimes, although there was a significantly greater survival in larynx than in pharynx plus dual tumours sites ($\chi^2 = 101.92$, $p \ll 0.0001$).

Tumour-free rates

The total number of recurrences that occurred in the 10 years from the start of treatment was 320; 159 patients and 161 patients in the 3F/wk and 5F/wk groups, respectively. The cumulative number of recurrences as a function of time are shown in Fig. 3.

In the Sixth and Seventh Interim Progress Reports (1978, 1982), analyses designated "recurrence-free rates" were adopted which were based on "no local recurrence". The wording has now been changed to "tumour free" to clarify that these patients had neither clinically detectable persistent tumour nor recurrent tumour at the primary site. "Tumour-free rates" represent the probability that a given patient has not suffered from either a persistent tumour or a recurrent tumour at the primary site at a specified time. Persistent tumour was counted as an event with zero survival time if the patient did not become tumour free as the result of the primary treament. Deaths without previous local recurrence or persistent tumour were counted as withdrawals

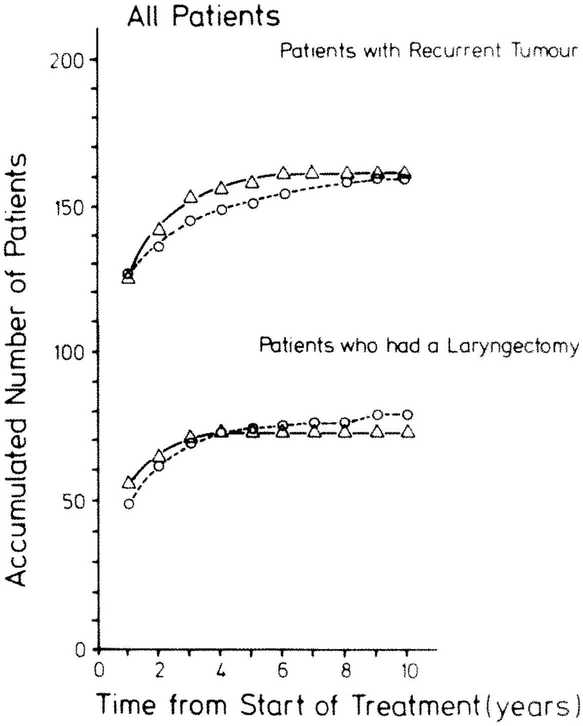

Figure 3. Accumulated number of patients who had a tumour recurrence or a laryngectomy *versus* time from start of radiation treatment for the 3F/wk and 5F/wk treatment groups. Symbols as in Fig. 1.

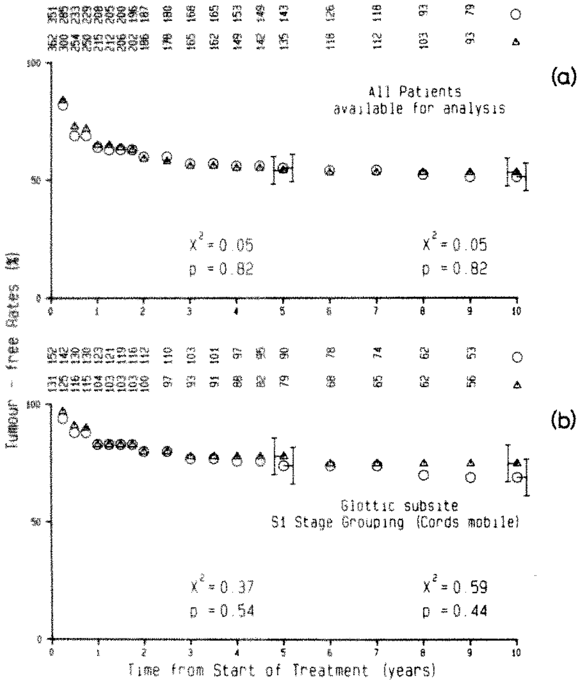

Figure 4. Tumour-free rates. (a) Percentage of all patients, except 21 exclusions, without persistent or recurrent tumour *versus* time from start of treatment. (b) Confined to patients in the glottic subsite, S1 stage grouping (cords mobile). Symbols as in Fig. 1.

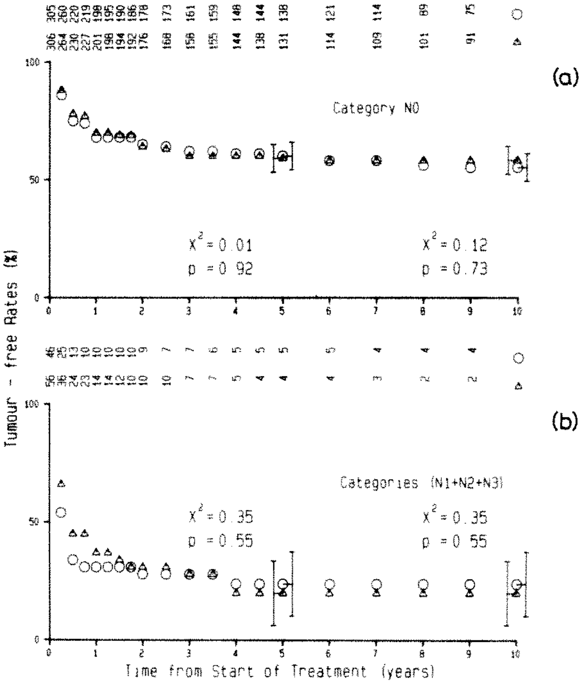

Figure 5. Tumour-free rates. (a) For patients who were in the N0 category at entry into the trial *versus* time from start of treatment. (b) For patients who were in the N1, N2 and N3 categories. Symbols as in Fig. 1.

at the time of death. The results based on these criteria are shown in Fig. 4a, where it can be seen that there was no statistically significant difference between the two arms. A multivariate analysis again found site and stage to be important independent prognostic variables. The relative risk (3F/wk to 5F/wk) for the treatment effect when included with these two factors was 1.14 with a 95% confidence interval of 0.92–1.43. This risk ratio was not significantly different from unity ($p = 0.22$).

When comparing the survival of patients who showed no sign of local recurrence, there had appeared to be a possibly statistically significant advantage in the 5F/wk group for the cords mobile sub-group because, at that time, inadequate weight was attached to the requisite diminution in p value associated with sub-group analyses (Sixth Interim Progress Report, 1978). This advantage had been greatly reduced and was not significant ($p = 0.17$) when the Seventh Interim Progress Report was written (1982). The current analysis (Fig. 4b) confirms this finding ($p = 0.44$). This suggested difference has never been seen previously in the sub-group other sites nor is it present there in the current analysis. Separate comparison of 3F/wk with 5F/wk in larynx sites and pharynx plus dual tumours sites also showed no significant differences between the two treatment arms (Table III).

The prognosis of patients will depend markedly on the initial nodal involvement; hence, sub-group analyses of tumour-free rates have been compared in the 3F/wk and 5F/wk treatment groups, firstly in patients who were classified as N0 at entry into the trial (Fig. 5a) and secondly in those classified as N1, N2 and N3 (Fig. 5b). In none of these analyses were any significant differences found between the two arms of the trial.

Laryngectomy-free rates

Laryngectomy-free rates were calculated with only the occurrence of a laryngectomy counting as an event. Deaths without previous laryngectomy were counted as withdrawals. The cumulative number of laryngectomies as a function of time are shown in Fig. 3. There were 151 laryngectomies in all, 79 and 72 in the 3F/wk and 5F/wk groups, respectively. It should be recognized by readers that not all patients are suitable for laryngectomy when they have a recurrence, and hence that the laryngectomy-free rates are not solely influenced by the initial randomization to 3F/wk and 5F/wk. Thus less reliance can be placed on laryngectomy-free data than on tumour-free data for judging the relative effectiveness of treatment in the two arms of the trial. Only four laryngectomies had to be performed as a result of radiation necrosis (Sixth Interim Progress Report, 1978). Neither tumour nor necrosis was reported in the pre- or post-laryngectomy histology reports in an additional 12 patients, four of whom had been treated with 3F/wk and eight with 5F/wk. All of these patients had had their laryngectomy before 3½ years from the start of their radiation treatment.

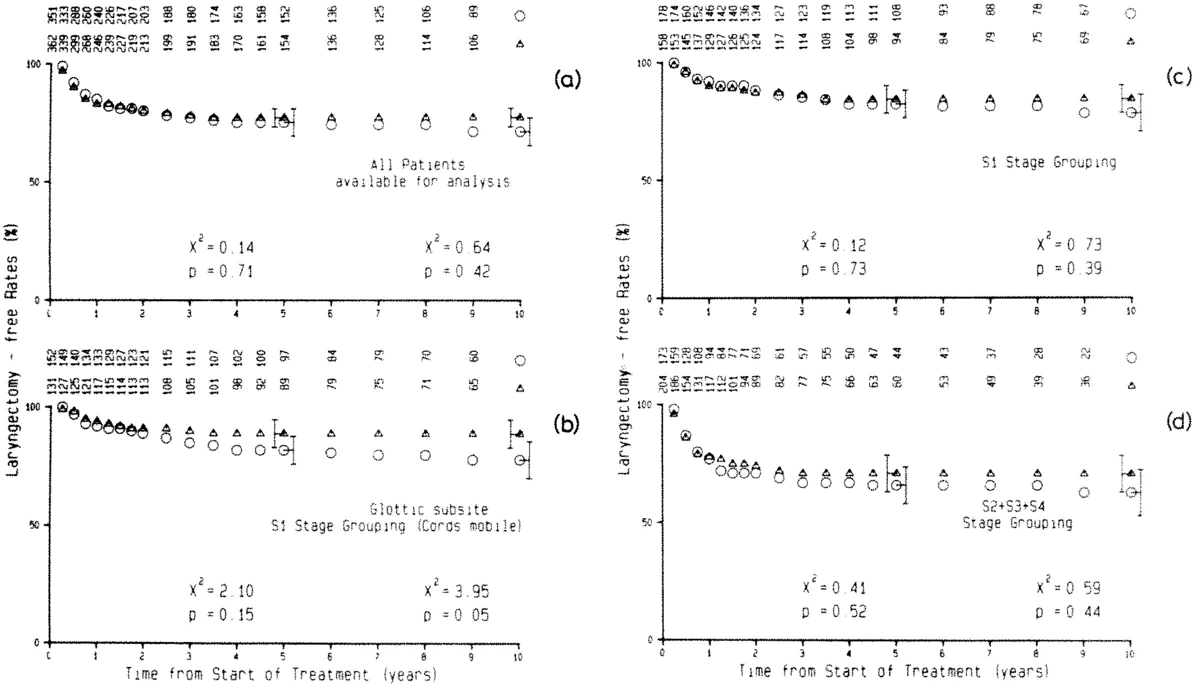

Figure 6. Laryngectomy-free rates. (a) Percentage of all patients, except 21 exclusions, surviving without having had a laryngectomy *versus* time from start of treatment. (b) For patients classified according to the previously used sub-group of cords mobile now designated glottic subsite S1 stage grouping. (c) Confined to patients in the S1 stage grouping. (d) For patients in the S2, S3 and S4 stage grouping. Symbols as in Fig. 1.

There were marginally fewer laryngectomies in the 3F/wk group than in the 5F/wk group in the first 3½ years but this trend was reversed in the period 3½ years to 10 years after start of treatment. In the latter period when there were no further laryngectomies in the 5F/wk group there were, nonetheless, still another nine recurrences in that group over that period whereas in the 3F/wk group there were eight laryngectomies performed for 13 recurrences which gives rise to the separation between the 3F/wk and the 5F/wk curves (Figs. 3 and 6). It can be seen that laryngectomy was only possible in 47% of patients who had a recurrence, that is in 151 patients out of 320 patients who had a recurrence.

When patients with tumours at all sites were analysed there were no significant differences in laryngectomy-free rates between the two treatment groups (Fig. 6a). This result was the same as previously reported (Sixth and Seventh Interim Progress Reports, 1978, 1982). The relative risk (3F/wk to 5F/wk) for the treatment effect in a multivariate analysis was 1.21 with a 95% confidence interval of 0.88–1.67, and this result was not significantly different from unity ($p = 0.27$). An apparent difference similar to that seen in the recurrence-free sub-group analyses, in favour of the 5F/wk treatment regime, was seen in the previous analyses for laryngectomy-free rates but only in the cords mobile sub-group. This was not surprising as the treatment for local recurrence at the primary site, when appropriate, is laryngectomy. With further follow-up (Fig. 6b), this difference has been slightly reduced but has not disappeared, with $p = 0.05$. In view of the uncertainties in the interpretation of sub-group analyses this result cannot be considered as evidence that a real difference exists (Tukey, 1977). Similarly, the differences in the sub-groups larynx and pharynx plus dual tumours (Table III) are also difficult to interpret and are referred to in the Discussion. Because the S1 category, which comprises both primary tumour and nodal status, is more appropriate than the previously adopted cords mobile sub-group, the data have been analysed accordingly (Fig. 6c). It can be seen that there is very little difference between the 3F/wk and 5F/wk treatment groups in the S1 analysis with no statistically significant difference at 10 years ($\chi^2 = 0.73$, $p = 0.39$).

For patients with more advanced tumours, that is in the S2, S3 and S4 categories, there is also no significant difference between the 3F/wk and the 5F/wk treatment groups (Fig. 6d). This was also the case for other sites in the previous interim reports (Sixth and Seventh Interim Progress Reports, 1978, 1982).

Normal-tissue effects

Acute reactions

Marked mucous membrane reactions were recorded in 94% and 96% of the patients in the 3F/wk and 5F/wk groups, respectively (Table IV). This is a clear indication that the two fractionation regimes being compared gave rise to similar acute reactions. Although

Table IV. Acute reactions in normal tissues up to 12 weeks after the start of radiotherapy treatment

Reaction	Number of patients with reactions	
	3F/wk	5F/wk
Patients analysed	351	362
Any kind of marked mucous membrane reaction		
At any time	331 (94%)	349 (96%)
Longer than 4 weeks	262 (75%)	304 (84)%
Marked mucous membrane reaction (ulceration or fibrinous)		
At any time	225 (64%)	258 (71%)
Longer than 4 weeks	47 (13%)	72 (20%)
Marked mucosal oedema		
At any time	132 (38%)	151 (42%)
Longer than 4 weeks	57 (16%)	69 (19%)
Marked skin reactions		
At any time	260 (78%)	284 (78%)
Longer than 4 weeks	98 (28%)	137 (38%)
Dysphagia		
At any time	216 (61%)	229 (63%)
Longer than 4 weeks	79 (22%)	113 (31%)
Perichondritis		
At any time	21 (6%)	22 (6%)
Longer than 4 weeks	6 (2%)	5 (1%)
Any kind of severe acute radiation reaction		
At any time	341 (97%)[a]	352 (97%)[a]
Longer than 4 weeks	280 (80%)[b]	320 (88%)[b]

Statistical comparison: $^a\chi^2 = 0.002$, $p = 0.96$; $^b\chi^2 = 1.57$, $p = 0.21$.

Table V. Late reactions in normal tissues after radiotherapy

Reaction	Number of patients with reactions	
	3F/wk	5F/wk
Patients analysed	351	362
Skin:		
Telangiectasia	13 (4%)	12 (3%)
Fibrosis and atrophy	30 (8%)	34 (9%)
Oedema	1 (0.3%)	2 (0.5%)
Dyspigmentation	29 (8%)	39 (11%)
Mucous membrane:		
Telangiectasia	58 (16%)	69 (19%)
Atrophy	16 (5%)	25 (7%)
Oedema	125 (36%)	134 (37%)
3–6 months	92 (26%)	107 (30%)
6–12 months	20 (6%)	15 (4%)
After 12 months	13 (4%)	12 (3%)
Cartilage:		
Perichondritis	7 (2%)	14 (4%)
Pain:		
In or outside treated area	26 (7%)	25 (7%)
Inside treated area	19 (5%)	16 (4%)
Probable myelitis:	1 (0.3%)	2 (0.5%)
Dysphagia:	39 (11%)	54 (15%)
All late reactions	208 (59%)[a]	225 (62%)[a]

Statistical comparison: $^a\chi^2 = 0.25$; $p = 0.62$.

more precise assessment of normal-tissue radiation reaction can be gained from the duration of the reaction, as distinct from the foregoing incidence of such reactions, the end points listed in Table IV serve only to illustrate the similarity of their incidence and duration because their inter-relationship and multiplicity makes it inappropriate to apply simple statistical handling to this data (Pocock, 1985; Pocock et al, 1987). Meaningful statistical evaluation can only be provided for the comparison of any type of severe acute radiation reaction between the two arms of the trial; neither the incidence nor the duration of such reactions showed any significant difference (Table IV).

Late reactions

Telangiectasia of the mucous membrane in the larynx is, clinically, a very difficult physical sign to evaluate as it requires indirect mirror examination. Thus only limited confidence should be placed on findings based on this parameter. However, the incidence was virtually the same in both arms of the trial (Table V). The other manifestations of late radiation damage in the mucous membrane, atrophy and oedema, were also similar in the 3F/wk and 5F/wk treatment groups. It was of particular interest that when oedema, of late onset, was examined in more detail with the breakdown of data according to the time of first appearance there was, even then, a similar distribution in both arms of the trial.

The incidence of late radiation damage in the skin was very small and, as previously reported, was commensurate with the quality of radiation used for treatment. Similarly, the other symptoms and signs of late radiation damage that were present were few in number and low in the degree of severity and were equally distributed between the two trial groups. This should not be misinterpreted as being an indication that the doses that were used were not high enough to cause significant late normal-tissue damage; the dose-limiting factor in the presently used treatment regimes was the acute normal-tissue radiation damage. In the late radiation reactions shown in Table V, for reasons stated above, it is only possible to perform useful statistical analyses on the incidence of any type of late reaction and these show no significant differences between the two arms of the trial ($\chi^2=0.25$, $p=0.62$).

Necrotic ulceration was considered in detail in the Sixth Interim Progress Report (1978) and there has been no further change in the data since that analysis. Records, based on a follow-up to death or a maximum

Table VI. Percentage survival related to nodal involvement at entry into trial, site and number of treatments per week

Site	N0				N1, N2 and N3			
	Larynx		Pharynx and dual tumours		Larynx		Pharynx and dual tumours	
(a) Both schedules combined								
Number of patients at entry	501		110		19		83	
Probability of surviving 3 years ±SE (%)	77±2		47±5		33±11		17±4	
Probability of surviving 5 years ±SE (%)	66±2		37±5		17±9		14±4	
Probability of surviving 10 years ±SE (%)	44±2		21±4		11±7		8±3	
	$\chi^2 = 37.62$, $p < 0.0001$				$\chi^2 = 0.98$, $p = 0.33$			
(b) For each fractionation schedule								
Treatments per week	3F	5F	3F	5F	3F	5F	3F	5F
Number of patients at entry	258	243	47	63	10	9	36	47
Probability of surviving 3 years ±SE (%)	75±3	78±3	40±7	52±6	34±16	33±16	20±7	15±5
Probability of surviving 5 years ±SE (%)	67±3	65±3	34±7	40±6	23±14	11±11	14±6	13±5
Probability of surviving 10 years ±SE (%)	43±4	45±4	27±7	17±5	11±11	11±11	11±5	6±4
	$\chi^2 = 0.01$, $p = 0.93$		$\chi^2 = 0.01$, $p = 0.93$		$\chi^2 = 0.03$, $p = 0.87$		$\chi^2 = 0.11$, $p = 0.79$	

Statistics refer to the comparison of survival rates for 3F/wk *versus* 5F/wk from entry into the trial to 10 years after treatment.

period of 10 years, show that only four of the reported necroses were attributable to radiation in excess of normal-tissue tolerance. These occurred within 1 year of treatment. In a further 11 patients reports of necrosis were made; however, subsequent events revealed that these were due to initial misinterpretation of tumour recurrence and were not due to excess radiation damage—a finding similar to that reported by Steward and Jackson (1975).

Discussion

For ethical reasons, interim analyses of data are a necessity for the early identification of clear-cut adverse reactions. These could indicate immediate amendment of the trial protocol or even the termination of entry into a trial. Fortunately no such trends were encountered in the present trial. It mus be remembered that the clinical assessment of the biological effectiveness of a given physical radiation dose is likely to be associated with a variation of ±5% at best. In order to justify the future use of a curtailed fractionation regime of 3F/wk as standard treatment, instead of the current clinical practice of using 5F/wk treatment schedules in the majority of radiotherapy centres, it has to be shown that equally good tumour cure rates can be achieved by treatment with 3F/wk for no greater normal-tissue radiation damage. Previous differences in survival rates have always been small whether analysis was made in the whole group of patients or in sub-groups. This final analysis, when all patients have been followed up for 10 years, confirms the previous findings when tumour cure is assessed in terms of observed survival rates (Figs 1 and 2) and tumour-free rates (Figs 4 and 5). The differences in survival rates were not statistically significant.

Tumour control

When a comparison was made between the patients who had a primary tumour at a laryngeal subsite and those who had a tumour involving a pharyngeal subsite then there was no difference in their survival whether they were treated with 3F/wk or with 5F/wk (Table III). However, there was a highly significant difference in the 3, 5 and 10 year survival probabilities between the laryngeal and pharyngeal sub-groups ($\chi^2 = 101.92$, $p \ll 0.0001$) (Table III). This throws doubt on the value of the conclusions that can be drawn from studies involving small numbers of patients whose tumours involved a variety of sites (Cox et al, 1980). This difference between laryngeal and pharyngeal tumours was also shown, more specifically, when the nodal status of these patients was taken into consideration. Patients with laryngeal tumours who had no enlarged lymph nodes on entry into the trial had a statistically better prognosis than similar patients with primary pharyngeal tumours (Table VI).

There was also a statistically significant difference in the incidence of patients with positive nodes between those in the laryngeal sub-group (4%) and those in the pharyngeal sub-group (49%) ($\chi^2 = 121.88$, $p < 0.0001$), but there was no significant difference between the latter sub-group and the dual tumours sub-group (41%) ($\chi^2 = 0.55$, $p = 0.45$). This finding is in accordance with previous reports in the literature (Lederman, 1970). However, when there were positive nodes present at the time of entry of the patient into the trial, then nodal involvement determined the survival of that patient, without any apparent influence on this by the site of the primary tumour or the fractionation regime used for the treatment (Table VI).

Since a patient with recurrence may be successfully salvaged by laryngectomy, measurement of survival is of only limited value in comparing local tumour control achieved by the two treatment regimes. However, it must also be recognized that laryngectomy cannot be offered to every patient who suffers a recurrence. In an earlier report (Sixth Interim Progress Report, 1978), there was a suggestion of more recurrences in patients treated by 3F/wk. This trend could not be demonstrated in the final analysis.

Similarly, in past reports the probability of laryngectomy tended to be higher in the 3F/wk group in a limited number of sub-group analyses. The final analysis shows that some apparent differences continue to exist. In the larynx sub-group there is an apparent advantage in the laryngectomy-free rates in favour of the 5F/wk group when compared with the 3F/wk group (Table III) but exactly the reverse is seen in the pharynx and dual tumours group. The differences in tumour-free rates in these two sub-groups (Table III) are much less and not at all statistically significant. Laryngectomy is only applicable for a limited number of patients with recurrence and this may have skewed the data for laryngectomy-free rates so that the statistics are difficult to interpret. There is also an increased risk of such apparently stastically significant differences being found when multiple analyses of sub-groups are performed (Pocock et al, 1987). It is therefore considered that the results in this sub-group analysis could well be due to random variation and may not represent a real effect of the primary treatments.

In our Sixth and Seventh Interim Progress Reports (1978, 1982), we speculated as to whether the biological effectiveness of the dose level chosen for 3F/wk might have been lower than that chosen for 5F/wk owing to the fact that different conversion factors apply for treatments given in a few fractions compared with treatments given in a large number of fractions (Wiernik, 1981). When considering dose per fraction, there was overlap between the two treatment arms. In a few cases patients given 3F/wk in long overall times received a dose per fraction similar to patients given 5F/wk in short overall times. The contributing centres may be divided into three groups, those using overall times of 3–4 weeks, those using between 4 and 6 weeks, and those using 6 weeks or more. The numbers of patients in each group were 216, 156 and 341, respectively. When these centres were coded 1 to 3 and the code included as a variable in the multivariate analyses, the variable was not significant and the estimates of relative risk for the treatment effect were virtually unchanged. However, there was a tendency for the difference in laryngectomy-free rates between 3F/wk and 5F/wk to decrease as the overall time increased, although the trend was not statistically significant ($p = 0.57$).

Normal-tissue damage

For a comparison of the relative degrees of normal-tissue damage, acute and late radiation damage have to be considered separately, as different biological mechanisms are involved in their development. However, up to the present time, they have in common that subjective methods of analysis have been used for their evaluation. Because the categorization of the lesser degrees of intensity of mucous membrane reaction are so arbitrary, a solution to this problem has been sought by adopting a simple classification of patients into those who had any marked degree of mucous membrane reaction and those who had not. A marked degree of radiation reaction involved either a fibrinous reaction that could go on to frank ulceration or an intense oedema. Both manifestations were recorded in the majority of patients (Table IV).

In the treatment of laryngeal carcinoma there is only a small separation between the parallel opposed treatment portals and, therefore, only moderate skin sparing was achieved with the use of megavoltage irradiation sources. Not surprisingly there was a high incidence of marked acute radiation reactions in the skin as well as in the mucous membrane which was similar in both arms of the trial. When the duration of the various parameters that were assessed, such as the marked mucous membrane reactions, skin reactions and dysphagia, was greater than 4 weeks, there was a marginally greater percentage of cases in the 5F/wk group, although little importance is attached to this finding. Other manifestations of acute radiation damage, such as mucosal oedema and perichondritis, were similar in both arms of the trial. The 6% incidence of perichondritis is an indication that the radiation doses used in this clinical trial were close to acute normal-tissue tolerance because an incidence of around 5% is the upper limit of this type of radiation damage that is acceptable to the majority of radiotherapists (Vermund, 1970). It must be stressed that in treatment regimes with photons, involving either 3F/wk or 5F/wk in an overall time varying between 3 and 6 weeks, the dose-limiting factor is acute normal-tissue tolerance and not late normal-tissue tolerance. With photon irradiation regimes similar to those used in this trial, the level of late normal-tissue damage that follows near maximum acute normal-tissue radiation damage is usually very modest (Fleming et al, 1961). Late reactions become the dose-limiting factor when either single fractions per week (Atkins, 1964) or high linear energy transfer (LET) radiations (Barendsen et al, 1979) are used.

At the time of planning the trial, in the early 1960s, it was decided that data on parameters such as skin reactions, dysphagia and perichondritis had to be collected since there were those who believed that regimes with curtailed fractionation would result in adverse normal-tissue radiation reactions and that such complications would be shown up through the study of these parameters (Preliminary Report, 1963; Second Progress Report, 1968). Examination of the final data concerning these parameters (Table IV) shows that there was no

Table VII. Time of first appearance of telangiectasia in the mucous membrane

Year	3F/wk (351 patients)		5F/wk (362 patients)	
	Number of patients with telangiectasia	Probability of not developing telangiectasia[a]	Number of patients with telangiectasia	Probability of not developing telangiectasia[a]
0–1	28	0.91	21	0.93
1–2	12	0.86	12	0.89
2–3	8	0.82	13	0.83
3–4	3	0.81	8	0.79
4–5	1	0.80	7	0.76
5–6	2	0.79	1	0.75
6–7	2	0.78	2	0.74
7–8	1	0.77	2	0.72
8–9	0	0.77	2	0.71
9–10	1	0.76	1	0.69
Total	58[b]		69[b]	

[a] Cumulative life table probabilities.
[b] Statistical comparison: logrank $\chi^2 = 0.62$, $p = 0.43$. No significant difference.

significant difference between them in the two trial groups when all types of severe acute normal-tissue reactions were compared.

Another legitimate fear was that curtailing the number of treatment fractions per week would result in unacceptable levels of late normal-tissue radiation damage. That these fears were well grounded has been shown by the results from a comparative trial of 3F/wk *versus* 5F/wk, in the treatment of carcinoma of the breast, in which similar total doses were used in both arms of the trial (Montague, 1967). In the present trial a dose reduction was made in the 3F/wk group compared with the dose given when 5F/wk were used for a similar overall time. No adverse incidence of late normal-tissue damage has been identified in this trial in any of the assessable tissues that have a large range of individual radiosensitivities (Table V) such as skin, mucous membrane, cartilage and central nervous tissue; neither could any difference be found in symptoms such as dysphagia or pain. An adverse difference might have been revealed when the times from the start of treatment to the first record of telangiectasia in the mucous membrane were compared in the two arms of the trial (Table VII) but even using this refined form of analysis no differences were found (Fleming et al, 1961).

Conclusion

Two different clinical, fractionated treatment regimes, given in the same overall time, were compared, one using the conventional 5F/wk and the other employing a curtailed number of 3F/wk. A dose reduction of 11–13% was made in the total dose used in the 3F/wk regime. The anatomical site chosen for this trial contained a variety of normal tissues that are considered to present most clinical problems in relation to different radiosensitivities. Despite this, the two regimes gave rise to similar and acceptable degrees of normal-tissue damage. Treatment with a curtailed number of fractions may offer social advantages for many patients with the additional benefit of being more economical. It is considered that this clinical trial, by investigating the safety of curtailed fractionation regimes for the treatment of squamous cell carcinoma of the laryngo-pharynx in terms of tumour control, patient survival and normal-tissue reactions, has provided valuable evidence on which a clinician can base his choice for future treatment policies.

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References

Preliminary Report of the Working Party of the British Institute of Radiology on the effects of dose fractionation in radiotherapy, 1963. *British Journal of Radiology*, *36*, 382–383.

Progress Report of the Working Party of the British Institute of Radiology: the effect of dose fractionation in radiotherapy, 1964. *British Journal of Radiology*, *37*, 562.

Second Progress Report of the British Institute of Radiology Fractionation Working Party, 1968. *British Journal of Radiology*, *41*, 723–724.

Third Progress Report on the British Institute of Radiology fractionation study on 3F/week or 5F/week treatment of larynx and pharynx, 1970. *British Journal of Radiology, 43,* 558–560.

Fourth Progress Report on the British Institute of Radiology fractionation study on 3F/week or 5F/week treatment of larynx and pharynx, 1971. *British Journal of Radiology, 44,* 211–213.

Fifth Progress Report on the British Institute of Radiology fractionation trial of 3F/week or 5F/week treatment of larynx and pharynx, 1972. *British Journal of Radiology, 45,* 754–756.

Sixth Interim Progress Report of the British Institute of Radiology fractionation study of 3F/week versus 5F/week in radiotherapy of the laryngo-pharynx, 1978. *British Journal of Radiology, 51,* 241–250.

Seventh Interim Progress Report of the British Institute of Radiology fractionation study of 3F/week versus 5F/week in radiotherapy of the laryngo-pharynx, 1982. *British Journal of Radiology, 55,* 505–510.

ALCOCK, C. J., FOWLER, J. F., HAYBITTLE, J. L., HOPEWELL, J. W., REZVANI, M. & WIERNIK, G., 1990. Salvage surgery following different fractionated radiation regimes for carcinoma of the laryngo-pharynx. *Clinical Otolaryngology,* (submitted).

ATKINS, H. L., 1964. Massive single dose, weekly fractionation technique in treatment of head and neck cancer. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 91,* 50–60.

BARENDSEN, G. W., BROERSE, J. J. & BREUR, K. (Eds) 1979. High-LET radiations in clinical radiotherapy (Pergamon Press, Oxford), pp. 43–50.

BARRETT, J. H., DAVY, T. J., DIXON-BROWN, A., GOODMAN, D., LAWSON, R. C., ORMSBY, P. L., SAUNDERS, J. E., WILLIAMS, P. C., FOWLER, J. F. & WIERNIK, G., 1990. Dosimetric intercomparison in the British Institute of Radiology fractionation study of 3F/week *versus* 5F/week in radiotherapy of laryngo-pharynx cancer. *British Journal of Radiology, 63,* 125–127.

COX, D. R., 1972. Regression models and life-tables. *Journal of the Royal Statistical Society, B, 34,* 187–220.

COX, J. D., BYHARDT, R. W., KOMAKI, R. & GREENBERG, M., 1980. Reduced fractionation and the potential of hypoxic cell sensitizers in irradiation of malignant epithelial tumours. *International Journal of Radiation Oncology, Biology and Physics, 6,* 37–40.

FLEMING, J. A. C. & WIERNIK, G., 1963. Influence of fractionation on clinical response and dosage in radiotherapy. *Nature (London), 199,* 924–925.

FLEMING, J. A. C., FILBEE, J. F. & WIERNIK, G., 1961. Sequelae to radical irradiation in carcinoma of the breast. *British Journal of Radiology, 34,* 713–719.

HAYBITTLE, J. L., ALCOCK, C. J., FOWLER, J. F., HOPEWELL, J. W., REZVANI, M. & WIERNIK, G., 1990. Recruitment, follow-up and analysis times in clinical trials of cancer treatment: a case study. *British Journal of Cancer,* (submitted).

JOHNS, M. E., NEAL, D. A. & CANTRELL, R. W., 1984. Staging of cervical lymph node metastases. Comparison of two systems. *Annals of Otology, Rhinology and Laryngology, 93,* 330–332.

LEDERMAN, M., 1970. Radiotherapy of cancer of the larynx. *Journal of Laryngology and Otology, 8,* 867–896.

MANTEL, N., 1966. Evaluation of survival data and two new rank order statistics arising in its consideration. *Cancer Chemotherapy Reports, 5,* 163–170.

MONTAGUE, E. D., 1967. Physical and clinical parameters in the management of advanced breast cancer with radiation therapy alone. *American Journal of Roentgenology, Radium Therapy and Nuclear Medicine, 99,* 995–1001.

POCOCK, S. J., 1985. Current issues in the design and interpretation of clinical trials. *British Medical Journal, 290,* 39–42.

POCOCK, S. J., HUGHES, M. D. & LEE, R. J., 1987. Statistical problems in the reporting of clinical trials. *New England Journal of Medicine, 317,* 426–432.

REZVANI, M., ALCOCK, C. J., FOWLER, J. F., HAYBITTLE, J. L., HOPEWELL, J. W. & WIERNIK, G., 1989. A comparison of the normal tissue reactions in patients treated with either 3F/week or 5F/week in the B.I.R. trial of radiotherapy for carcinoma of the laryngo-pharynx. *International Journal of Radiation Biology, 56,* 717–720.

—— 1990. Results of the first B.I.R. study of 3F/week versus 5F/week in radiotherapy of carcinoma of the laryngo-pharynx: normal tissue reactions. *International Journal of Radiation Oncology, Biology, Physics,* (submitted).

STEWART, J. G. & JACKSON, A. W., 1975. The steepness of the dose response curve both for tumour cure and normal tissue injury. *The Laryngoscope, 85,* 1107–1111.

TUKEY, J. W., 1977. Some thoughts on clinical trials, especially problems of multiplicity. *Science, 198,* 679–684.

UICC, 1968. *TNM Classification of Malignant Tumours,* 1st edn (International Union Against Cancer, Geneva).

UICC, 1978. *TNM Classification of Malignant Tumours,* 3rd edn (International Union Against Cancer, Geneva).

UICC, 1987. *TNM Classification of Malignant Tumours,* 4th edn (International Union Against Cancer, Springer-Verlag, London).

VERMUND, H., 1970. Role of radiotherapy in cancer of the larynx as related to the TNM system of staging. *Cancer, 25,* 485–504.

WIERNIK, G., 1980. Lessons from a multicentre clinical trial monitoring tumour and normal tissue response quantitatively. *British Journal of Cancer, Suppl. IV, 41,* 51.

WIERNIK, G., 1981. Three or five times weekly fractionation—evidence from the B.I.R. fractionation survey of laryngeal carcinoma. *British Journal of Radiology, 54,* 170–171.

WIERNIK, G., ALCOCK, C. J., FOWLER, J. F., HAYBITTLE, J. L., HOPEWELL, J. W. & REZVANI, M., 1990. The predictive value of tumour classification compared with the results of the British Institute of Radiology fractionation trial in the treatment of carcinoma of the laryngo-pharynx. *The Laryngoscope,* (in press).

WIERNIK, G., REZVANI, S. M. & MEMBERS OF BIR FRACTIONATION WORKING PARTY, 1988. Final results of the first B.I.R. fractionation survey in treatment of cancer of laryngopharynx. *Clinical Radiology, 39,* 354.

WIERNIK, G., REZVANI, M. & MEMBERS OF THE BIR FRACTIONATION WORKING PARTY, 1989. British Institute of Radiology studies of dose fractionation in radiotherapy for tumours of the laryngo-pharynx. *British Journal of Radiology, 62 (Congress Supplement),* S50.

1990, *The British Journal of Radiology*, *63*, 181–185

Anatomical variations of the carotid bifurcation: implications for digital subtraction angiography and ultrasonography

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Abstract. Intravenous digital subtraction angiography was used to determine prospectively the positional variations of the common carotid bifurcation in 100 consecutive patients with clinically suspected arteriosclerotic disease. The most common position (97/200, 48.5%) of the external carotid artery was anteromedial to the internal carotid artery. Position of the external carotid artery anterolateral to the internal carotid artery was noted in 26/200 (13%) bifurcations, but this anatomical variant was more common on the right (21/100) than on the left (5/100) ($p < 0.01$). Practical implications may be drawn from this study. For digital subtraction angiography, the left anterior oblique view has to be considered the projection of choice and the right common carotid bifurcation is less likely to be adequately displayed than the left one; for duplex ultrasonography, optimal visualization is obtained from a posterolateral orientation of the transducer.

In non-selective intra-arterial (IA) or intravenous (IV) digital subtraction angiography (DSA) of the common carotid artery bifurcations, the lateral projection cannot be used: both carotid arteries fill simultaneously on injection of contrast material and consequently superimpose on each other. As described in neuroradiological textbooks (Dilenge & Heon, 1974; Taveras & Wood, 1976), the external carotid (EC) artery is typically anteromedial to the internal carotid (IC) artery; therefore, the oblique projections (right anterior oblique (RAO) and left anterior oblique (LAO)) are adequate to assess the majority of carotid bifurcations (Chilcote et al, 1981; Kaseff, 1982) as the right carotid bifurcation is clearly displayed on the RAO view and the left carotid bifurcation on the LAO view, moreover projected over the cervical spine, where laryngeal artifacts due to swallowing are not a problem (Fig. 1). However, owing to anatomical variants, superimposition of the IC artery upon the EC artery on these ipsilateral oblique views is a quite common observation (up to 38%) (Kaseff, 1982).

In the literature concerning duplex sonography of the extracranial carotid arteries, it is considered that the EC artery lies anterior to the IC artery, but that in 5% of patients the antero-posterior orientation of the IC artery and EC artery is reversed (Dreisbach et al, 1983; Bluth et al, 1986); in addition, it is sometimes difficult to identify on real-time imaging the relationship of the IC artery to the EC artery. In particular, massive calcified plaques may cause sufficient shadowing to interfere with sonographic evaluation of the bifurcations and to induce diagnostic misinterpretations (Prendes et al, 1980). Therefore, knowledge of the anatomical variants of the carotid bifurcation is essential for accurate interpretation.

This prospective study reviews the radioanatomy of the carotid bifurcations and defines practical implications for DSA and Doppler ultrasonography.

Materials and methods

Between September and December 1987 intravenous DSA of the extracranial carotid arteries was performed on 108 consecutive adult patients with clinically suspected cerebrovascular disease. Eight patients were excluded from the study, as the observers agreed that image quality was inadequate (motion and swallowing artifacts in six; contrast resolution in two). The remaining 100 patients included 50 males and 50 females; average age was 65 years (range 40–84 years; mean for females, 67 years and for males, 63 years), yielding 200 carotid bifurcations (100 right and 100 left).

The DSA system consisted of a digital vascular imager (Philips) incorporated in a standard angiography system (matrix 512 × 512); a 25 cm image intensifier was used routinely. All patients received a bolus injection of 40 ml of low ionic contrast medium (Hexabrix, 320 mg iodine/ml) via a 16 gauge needle placed in the basilic or cephalic vein, at a rate of 12–14 ml/s.

Routine evaluation consisted of at least three views, centred on the carotid bifurcations, one LAO, one frontal and one RAO view. Oblique views were obtained (Chilcote et al, 1981), with the X-ray tube angled 25°, and the patient's head angled 40°, for a total angulation of 65°. Oblique projections were referred to as "ipsilateral oblique" when the patient's head was turned 40° opposite to the side of the concerned carotid bifurcation; "contralateral oblique" indicated that the patient's head was turned 40° towards the side being considered.

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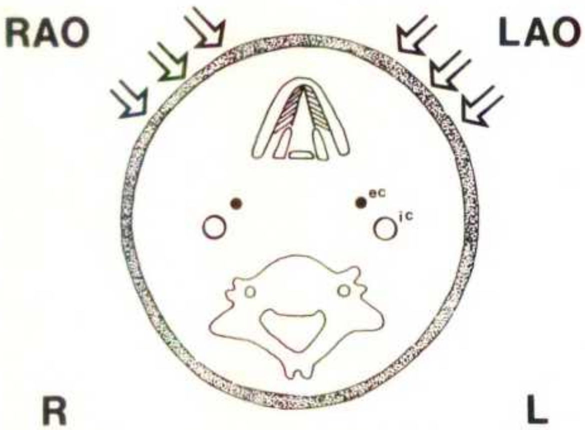

Figure 1. Schematic drawing showing classical ECAM (external carotid anteromedial) bifurcations: the right and left carotid bifurcations are projected over the cervical spine, avoiding swallowing artifacts, and adequately opened without vessel superimposition, respectively in the RAO and LAO projections (ec = external carotid artery, ic = internal carotid artery).

By assessment of the positional variations of the IC and EC arteries on these three views, it was possible to determine the position of the EC artery in relation to the IC artery, using a logical algorithm (Fig. 2). The results were classified into eight anatomic variants: (1) external carotid anterior (ECA), (2) external carotid anteromedial (ECAM), (3) external carotid medial (ECM), (4) external carotid posterior (ECP), (5) external carotid lateral (ECL), (6) external carotid anterolateral (ECAL), (7) external carotid posteromedial (ECPM), and (8) external carotid posterolateral (ECPL) (Figs 2 and 3).

The incidence of these anatomical variants was tabulated for both the left and right bifurcations together, and subsequently for the right and left bifurcation considered separately. The theoretically more relevant projections for adequate demonstration of the carotid bifurcations were consequently determined. In addition, the number (0, 1, 2) of different projections (LAO, RAO, frontal) on which the proximal IC artery could be correctly assessed was tabulated independently by two observers, taking into account not only vessel overlap-

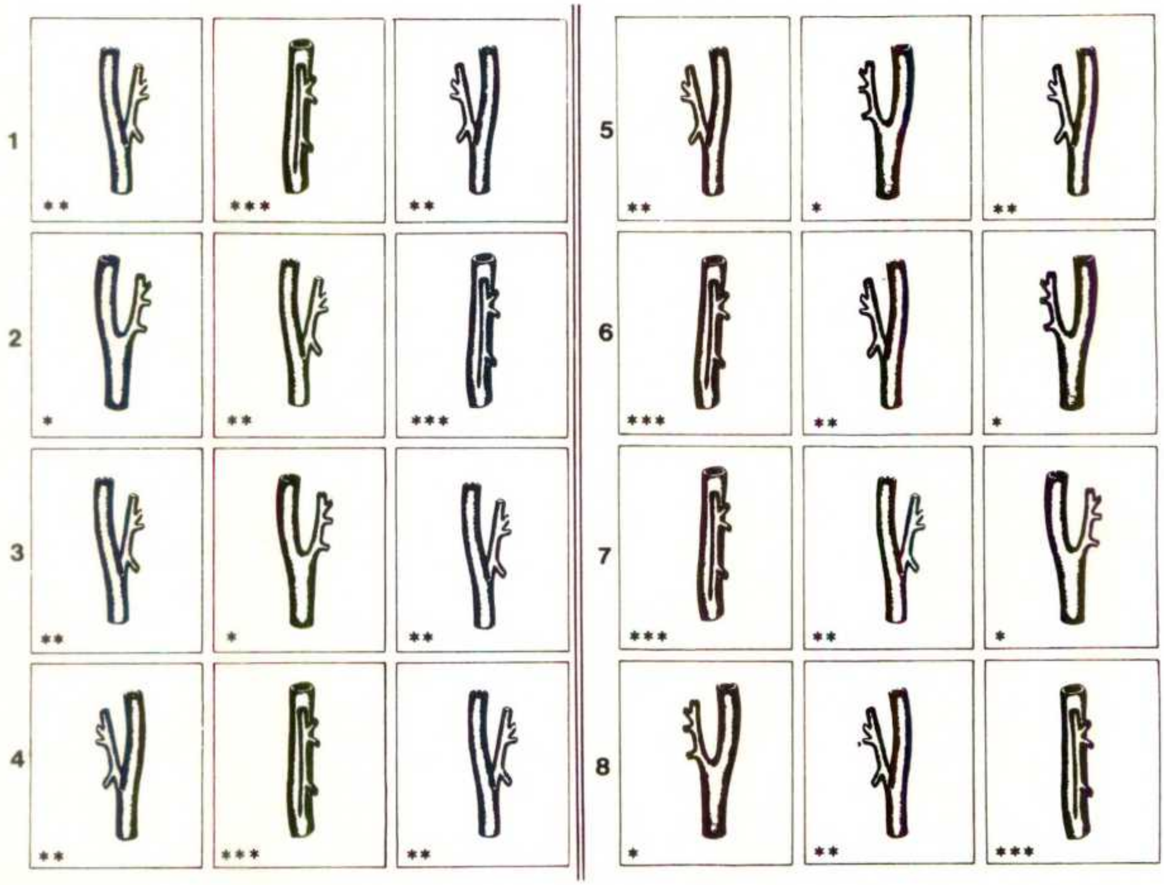

Figure 2. Algorithm used to evaluate the relationship between the right EC and IC arteries (*, the bifurcation is ideally opened; **, the bifurcation is adequately opened; ***, vessel superimposition). 1, ECA; 2, ECAM; 3, ECM; 4, ECP; 5, ECL; 6, ECAL; 7, ECPM; 8, ECPL).

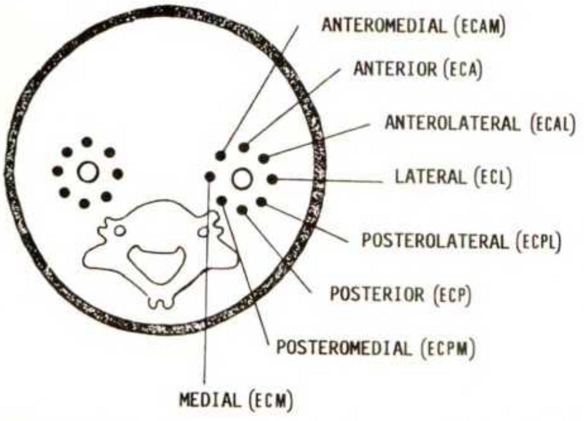

Figure 3. Schematic drawing representing the eight anatomical variants considered.

ping, but also all other possible causes for failure, in particular motion and swallowing artifacts (Chilcote et al, 1981); when the observers disagreed, the views were re-examined and a consensus opinion was reached. Chi-square tests were used for data analysis.

Results

The ECAM, ECA and ECAL variants were found in 97/200, 69/200 and 26/200 respectively cases for a total of 192/200 cases (96%), (Table I). A statistically relevant difference ($p < 0.01$) between the right and left bifurcations was observed. The ECAL variant, rather common on the right (21/100) was infrequent on the left (5/100).

For geometrical reasons, the LAO projection can open ideally or adequately (see Fig. 3) the ECA, ECL, ECPL, ECP, ECM and ECAM variants of the left bifurcation and the ECA, ECM, ECPM, ECP, ECL, ECAL and ECA variants of the right bifurcation: according to our distribution pattern (see Table I), 159/200 bifurcations (80%). The RAO projection can profile the ECA, ECL, ECPL, ECP, ECM and ECAM right bifurcations and the ECA, ECM, ECPM, ECP, ECL, ECAL and ECA left bifurcations: 116/200 bifurcations (58%). The frontal projection can profile the ECAL, ECL, ECPL, ECPM, ECM, ECAM left and right bifurcations: 131/200 bifurcations (65%).

Finally, considering all parameters including vessel superimposition, contrast resolution, swallowing and motion artifacts, the ostium of the IC artery could be assessed on at least two projections in 74% of the patients with the ECA or ECAM variants, whereas in ECAL variants it could be evaluated on two projections in only 19% of the cases. This difference is statistically highly significant ($p \ll 0.001$) (Table II).

Discussion

Our study shows that, as classically reported in the literature (Dilenge & Heon, 1974; Taveras & Wood, 1976; Kaseff, 1982), the most frequent variant is the ECAM (97/200, 48.5%). It also appears that the lateral variants (ECL, ECPL, ECAL) are encountered in up to 16% of cases. This observation, which contrasts with classical descriptions, had already been reported in a case report (Jyoji et al, 1972) and in two larger series, though with a lesser frequency than in our experience, 5.3% (Prendes et al, 1980) and 11.4% (Teal et al, 1973). Moreover, the present study demonstrates that there are statistically significant differences between the anatomical distributions of the right and left carotid bifurcation. The ECAL variant, in particular, appears to be infrequent on the left (5/100) and much more common on the right (21/100). To our knowledge, this has only been reported in a large series by one author (Teal et al, 1973), but practical conclusions were not drawn.

Implications for digital subtraction angiography (DSA)

1. The LAO projection is potentially the best suited to assess reliably the carotid bifurcation both on the right and left side (80% of the cases), whereas the RAO view would adequately profile 58% and the frontal view 65% of the bifurcations. Practically, an LAO projection should be the first in all DSA examinations and should be repeated preferably to any other when motion or swallowing artifacts interfere and in case of superimposition by the vertebral arteries or inadequate timing in serial imaging.

2. The right bifurcation is likely to be less adequately profiled on DSA than the left one. It is usually consid-

Table I. Distribution of the eight anatomical variants

	Right + left bifurcations $n = 200$	Right bifurcation $n = 100$	Left bifurcation $n = 100$
External carotid anterolateral (ECAL)	26 (13%)	21*	5*
External carotid lateral (ECL)	4 (2%)	4	0
External carotid anterior (ECA)	69 (34·5%)	40	29
External carotid antero-medial (ECAM)	97 (48.5%)	34	63
External carotid posterolateral (ECPL)	2 (1%)	1	1
External carotid posteromedial (ECPM)	1 (0.5%)	0	1
External carotid medial (ECM)	1 (0.5%)	0	1
External carotid posterior (ECP)	0 (0%)	0	0

*$p < 0.01$.

ered that evaluation of the degree of stenosis requires assessment of the ostium of the IC artery on at least two projections (Hoffman et al, 1983). With the ECAL variant, the carotid bifurcation is statistically less easily interpretable on two projections than with the ECAM or ECA variants (two projections are interpretable in 19% of the cases with ECAL against 74% with ECAM and ECA). In our opinion, this difference is largely due to the fact that with the ECAL variant the bifurcation is satisfactorily profiled only on the contralateral oblique view (LAO for the right bifurcation and RAO for the left bifurcation) in superimposition upon the larynx, a projection that increases the possible occurrence of swallowing misregistration artifacts. As there is a greater incidence of the ECAL variant on the right side (21% against 5% on the left), we conclude that the right carotid bifurcation is less likely to be adequately analysed on two projections than the left one.

These implications are particularly relevant regarding intravenous DSA, as with this procedure swallowing artifacts are frequently encountered and the use of large volumes of contrast material is a major drawback limiting the number of runs that can be performed (Pelz et al, 1985). Intravenous DSA is a procedure which is infrequently used now, but these implications are also true for non-selective intra-arterial DSA which may also be hampered, though to a lesser extent, by swallowing misregistration artifacts and may in some instances be impeded by a limited amount of contrast material, as these intra-arterial procedures are sometimes associated with simultaneous investigation of other anatomical areas.

Implications for ultrasonography

For the demonstration of the carotid bifurcations, anterior and posterior orientations of the transducer are not used, as the artery is too deep for the short-focus, high frequency transducers used for carotid arteries.

According to our study, we recommend the posterolateral approach, because it uses favourably the sternocleidomastoid muscle as an acoustic window (Grant et al, 1988) and because the carotid nearest the transducer is the IC artery in 96% of the cases (ECAL + ECA + ECAM + ECM) (see Table I). Also, using the posterolateral approach, it is theoretically possible to visualize both the IC and EC arteries on the same longitudinal plane in the ECAM variant (Fig. 4), that is, in up to 48% of the cases (63% on the left and 34% on the right) (see Table I). This simultaneous view of the IC and EC arteries is advantageous. From a posterolateral approach, when one carotid only is visualized on the longitudinal scan, if the Doppler examination identifies it as the IC artery, the EC artery has to be searched for by a slight anterior rotation movement of the probe (Fig. 5). Similarly, if the artery shown on the longitudinal scan is identified with Doppler as the EC artery, the transducer has to be slightly moved backwards to detect the IC artery.

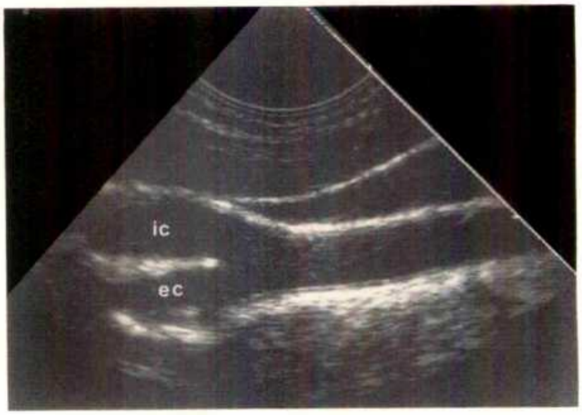

Figure 4. Longitudinal scan through a right carotid bifurcation: simultaneous visualization of both the internal (ic) and external (ec) carotid arteries.

The anterolateral approach does not benefit from the acoustic window provided by the sternocleidomastoid muscle and simultaneous visualization of the IC and EC arteries on a longitudinal scan is theoretically possible only in case of ECAL variant, that is, in 13% of the cases (21% on the right and 5% on the left) (see Table I). From a strictly lateral approach, the EC artery is the nearest to the transducer in 16% of cases (ECL + ECPL + ECAL), the most distal in 49% (ECAM + ECM + ECPM), and both arteries are at the same level in 35% of cases (ECA + ECP). Additionally, an important variability between the right and the left side should be expected (see Table I). Identification of the carotid arteries is consequently particularly difficult on the sole basis of anatomical data, and visualization of both arteries simultaneously on a longitudinal scan

Table II. Number of diagnostic projections†

	ECA $n = 69$	ECAM $n = 97$	ECAL $n = 26$	ECA + ECAM $n = 166$	Right $n = 100$	Left $n = 100$
Two diagnostic projections	52 (75%)	70 (72%)	5 (19%)*	122 (74%)*	61 (%)	72 (%)
One diagnostic projection	11 (16%)	24 (25%)	12 (46%)	35 (21%)	25 (%)	25 (%)
No diagnostic projection	6 (9%)	3 (3%)	9 (35%)	9 (5%)	14 (%)	3 (%)

*$p \ll 0.001$.

†Number of different projections (LAO, RAO, front) by patient, from which configuration of the proximal IC artery could be correctly assessed, considering the three most common variants (ECA, ECAM, ECAL).

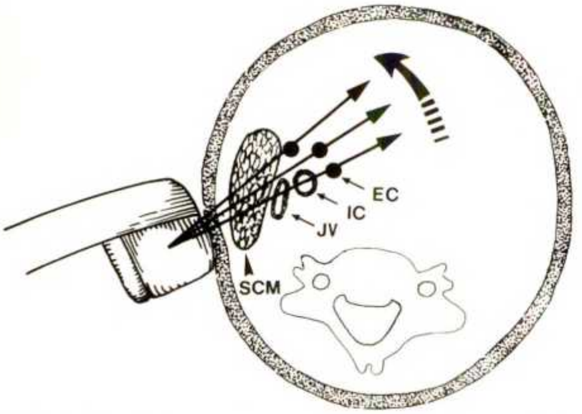

Figure 5. Rotation movement of transducer. In this case for the detection of the EC artery when the IC artery has been identified by Doppler examination (JV = jugular vein; SCM = sternocleidomastoid muscle).

can only be obtained in theory in 2% of cases (ECL or ECM variant) (see Table I); this lateral approach is consequently not recommended, though it can also use the sternocleidomastoid muscle as an acoustic window.

In summary, for DSA examination of the carotid bifurcations, the LAO view is the projection of choice, although the right carotid bifurcation is probably less easily interpretable than the left. For duplex ultrasonography the best orientation of the transducer is posterolateral.

References

BLUTH, E. I., KAY, D., MERRITT, C. R., SULLIVAN, M., FARR, G., MILLS, N. L., FOREMAN, M., SLOAN, K., SCHLATER, M. & STEWART, J., 1986. Sonographic characterization of carotid plaque: detection of hemorrhage. *American Journal of Roentgenology, 146*, 1061–1065.

CHILCOTE, W. A., MODIC, M. T., PAVLICEK, W. A., LITTLE, J. R., FURIAN, A. J., DUCHESNEAU, P. M. & WEINSTEIN, M. A., 1981. Digital subtraction angiography of the carotid arteries: a comparative study in 100 patients. *Radiology, 139*, 287–295.

DILENGE, D. & HEON, M., 1974. The internal carotid artery. In *Radiology of the Skull and Brain*, ed. by T. H. Newton (Mosby, St Louis), pp. 1202–1245.

DREISBACH, J., SEIBERT, C. E., SMAZAL, S. F., STAVROS, A. T. & DAIGLE, R. J., 1983. Duplex sonography in the evaluation of carotid artery disease. *American Journal of Neuroradiology, 4*, 678–680.

GRANT, E. G., WONG, W., TESSLER, F. & PERRELLA, R., 1988. Cerebrovascular ultrasound imaging. *Radiologic Clinics of North America, 26*, 1111–1130.

HOFFMAN, M. G., GOMES, A. S. & PAIS, S. O., 1983. Limitations in the interpretation of intravenous digital subtraction angiography. *American Journal of Roentgenology, 140*, 855–859.

JYOJI, H., MASAYUKI, M. & HAJIME, H., 1972. Lateral position of the external carotid artery: report of a case. *Radiology, 102*, 361–362.

KASEFF, L. G., 1982. Positional variations of the common carotid artery bifurcation: implications for digital subtraction angiography. *Radiology, 145*, 377–378.

PELZ, D., FOX, A. J. & VINUELA, F., 1985. Oblique positioning for intravenous digital subtraction angiography images of the neck and head. *Journal of the Canadian Association of Radiologists, 36*, 37–40.

PRENDES, J. L., MCKINNEY, W. M., BUONANNO, E. S. & JONES, A. M., 1980. Anatomic variations of the carotid bifurcation affecting Doppler scan interpretation. *Journal of Clinical Ultrasound, 8*, 147–150.

TAVERAS, J. M. & WOOD, E. H., 1976. *Diagnostic Neuroradiology*. (Williams and Wilkins, Baltimore), pp. 577–578.

TEAL, J. S., RUMBAUGH, C. L., BERGERON, R. T. & SEGALL, H. D., 1973. Lateral position of the external carotid artery: a rare anomaly? *Radiology, 108*, 77–81.

1990, *The British Journal of Radiology*, *63*, 186–189

"Diaphragm-like" strictures of the small bowel in patients treated with non-steroidal anti-inflammatory drugs

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Abstract. The radiological findings are described in four patients who developed strictures of the small bowel, and who had received non-steroidal, anti-inflammatory drugs (NSAIDs) for 1.5–15 years. Clinical presentation was that of subacute small bowel obstruction. Small bowel barium studies showed multiple discrete strictures. Some strictures were indistinguishable from those of regional enteritis. Others however were narrow "diaphragm-like" septae encroaching on and markedly narrowing the ileal lumen, and shown histologically to be due to submucosal fibrosis. It is suggested that these strictures are likely to be consequent on NSAIDs administration and that radiologists and surgeons need to be aware of these "diaphragms" which can be very difficult to detect on barium examination, either small bowel follow-through or enteroclysis, and at laparotomy.

It is now recognized that non-steroidal anti-inflammatory drugs (NSAIDs) can, in addition to their well-known effects on the gastroduodenal mucosa, also cause small intestinal damage. This damage manifests itself in a variety of ways, including malabsorption (Kendall & Hawkins, 1971; Dyer et al, 1971), permeability changes (Bjarnason & Peters, 1984), blood and protein loss (Bjarnason et al, 1987a), and inflammation (Bjarnason et al, 1987b). We present the findings in four patients who developed small bowel strictures. Some of these strictures are very short and may be difficult to detect on barium studies and at surgery.

Case reports

Case 1

A 40-year-old female with rheumatoid arthritis had been treated with several different NSAIDs for 15 years, but on admission was taking aspirin and azapropazone. She was admitted complaining of recurrent abdominal pain. She was hypoalbuminaemic. A ^{111}In-labelled leucocyte scan showed significant small intestinal inflammation (Fig. 1) and a barium follow-through showed two areas of ileal stricturing (Fig. 2). These strictures were long and radiologically indistinguishable from changes found in regional enteritis. Gastroscopy, barium enema and colonoscopy were normal. At laparotomy the serosal appearance of the small bowel was normal, but on palpation there were several strictures over a length of 120 cm. There was no obvious obstruction. The surgeon considered that Crohn's disease was the likely diagnosis, and decided against biopsy or resection of bowel. An enlarged mesenteric lymph node was biopsied and showed benign reactive changes only.

During the next 2 years the patient experienced increasingly frequent episodes of subacute intestinal obstruction. She eventually underwent elective laparotomy, when multiple, short constrictions were apparent and 50 cm of small bowel was resected. When the bowel was opened it was found that the strictures were very short, like "diaphragms" encircling the bowel and reducing the lumen to 1 mm in some areas. At pathological examination 19 such separate strictures were found and histology showed these to represent discrete fibrotic bands. There were no granulomas nor any other feature of Crohn's disease.

Case 2

A 70-year-old female was admitted for investigation of fatigue, weight loss (20 kg in 4 months), colicky

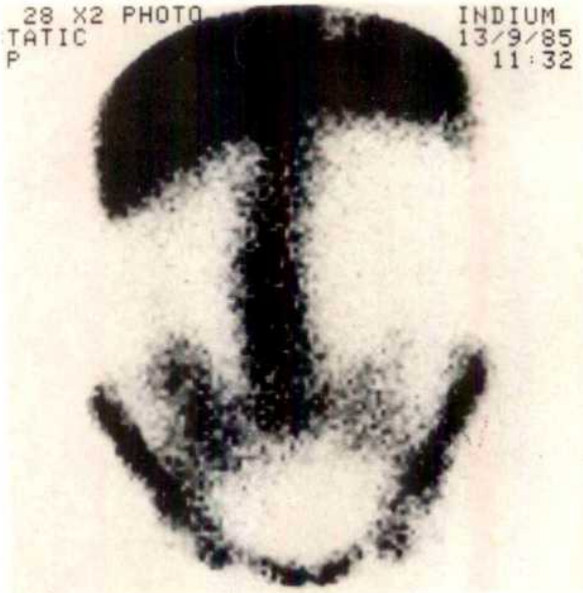

Figure 1. *Case 1.* ^{111}In-labelled autologous leucocyte scan. There is late abnormal localization of label in the right iliac fossa, indicating small bowel inflammation, with resulting excretion of label in the small bowel lumen and migration to the caecum.

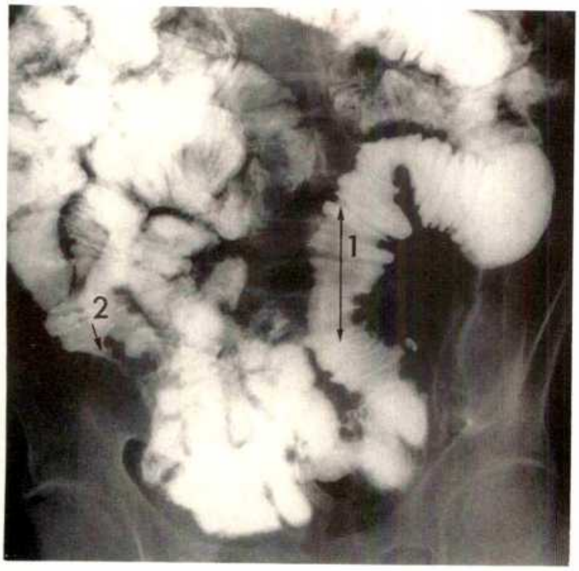

Figure 2. *Case 1.* Small bowel barium follow-through. The two strictured areas (1) and (2) and were persistent and radiologically indistinguishable from those of Crohn's disease.

abdominal pain, iron deficiency anaemia and hypoalbuminaemia. She had osteoarthritis for which she had been taking piroxicam for 18 months. Small bowel enema showed at least six diaphragm-like strictures (Fig. 3). At laparatomy a 60 cm length of bowel, commencing 70 cm distal to the ligament of Trietz was found to contain at least 30 luminal narrowings. This length of bowel was resected (Fig. 4), and the histological features (Fig. 5) of the narrow, discrete strictures were identical to those in Case 1.

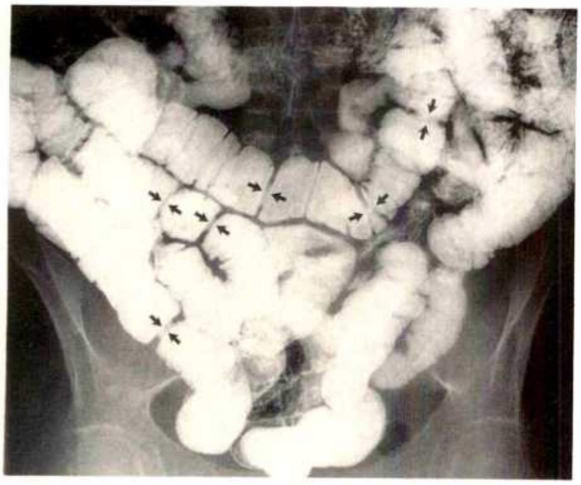

Figure 3. *Case 2.* Enteroclysis. The arrows indicate the position of strictures subsequently found in a 70 cm length of resected intestine. The mucosa adjacent to these very tight strictures appeared radiologically normal. Some of these 'diaphragms' were so tight that they narrowed the diameter of the lumen to 1–3 mm.

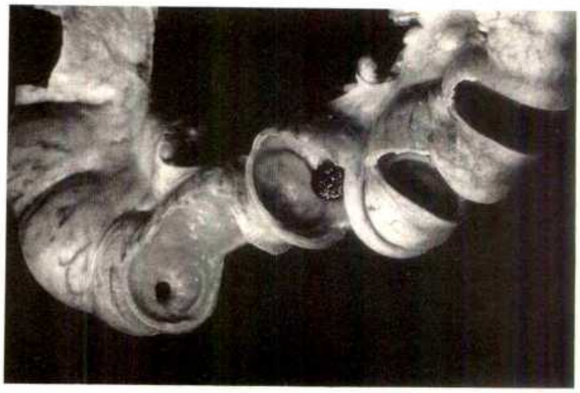

Figure 4. *Case 2.* Excised ileum showing multiple 'diaphragms' dividing the small intestine into segments. The bowel was prepared by inflating with formalin and cutting out several windows to show the compartments. One of these compartments contains an 'enteric-coated' tablet.

Case 3

A 40-year-old male gave a 1 year history of intermittent abdominal pain with bloating, diarrhoea and vomiting. He had been taking phenylbutazone for 3 years because of low back pain. Small bowel enema showed a persistent narrowing of the terminal ileum, with proximal dilatation. There was suspicion of a second stricture 17 cm proximal to the ileocaecal valve. At laparotomy the only abnormality to be seen was a terminal ileal stricture with proximal dilatation, which did not appear inflamed. A standard right hemicolectomy was performed. On opening the resected small bowel, small aphthoid-like ulcers were seen in the terminal ileum. In addition a stricture was present at the ileocaecal valve with mucosal atrophy but no ulceration. Histological examination showed submucosal fibrosis extending throughout the full thickness of the muscle

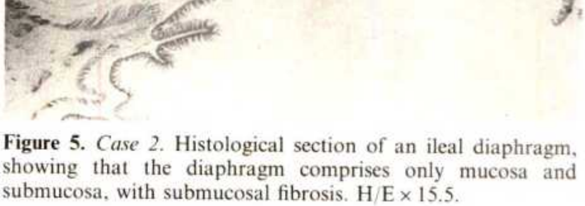

Figure 5. *Case 2.* Histological section of an ileal diaphragm, showing that the diaphragm comprises only mucosa and submucosa, with submucosal fibrosis. H/E × 15.5.

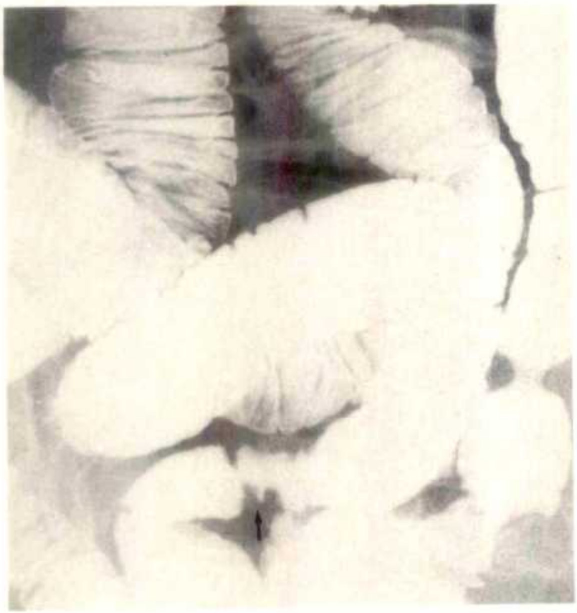

Figure 6. *Case 4.* Enteroclysis, showing a single discrete ileal stricture. The rest of the small bowel showed no other abnormality.

coat, with no evidence of Crohn's disease or tuberculosis.

Case 4

A 65-year-old female presented with a short history of diarrhoea. Over the ensuing months she lost weight and became hypoalbuminaemic. She had been taking naproxen for several years for cervical osteoarthritis. Barium follow-through showed the distal jejunum and the whole of the ileum to have thickened folds, but no ulceration or strictures. At laparotomy no major intestinal pathology was noted, but serosa looked hyperaemic and oedematous. An ileal biopsy showed non-specific ileitis only, and an enlarged mesenteric lymph node showed reactive follicular hyperplasia. Her medication with NSAIDs was stopped and her symptoms subsided within 4 months. A year later a small bowel barium enema (Fig. 6) showed a discrete ileal stricture but an otherwise normal small bowel. The patient was then, and still remains, asymptomatic.

Discussion

Evidence that NSAIDs can seriously damage the small intestine is now well established. Xylose and fat malabsorption has been demonstrated in patients with arthritis treated with NSAIDs (Kendall & Hawkins, 1971; Dyer et al, 1971). More recently it has been shown that NSAIDs disrupt intestinal integrity and increase intestinal permeability (Bjarnason & Peters, 1984). Small intestinal inflammation has been demonstrated with the use of ^{111}In-labelled leucocyte scans (Bjarnason et al, 1987b), and this inflammation has been shown to result in significant blood and protein loss (Bjarnason et al, 1987a). Madhok et al (1986) described three cases of small intestinal ulcers in patients taking NSAIDs. There have also been other isolated reports of small intestinal ulcers, and also of strictures in patients on NSAIDs (Longstrieth & Newcomer, 1975; Neoptolemos & Locke, 1983; Saverymuttu et al, 1986). Interestingly, it is noted (in retrospect) that some of the patients in Davies and Brightmore's (1970) description of potassium-induced ulceration of the small intestine were also taking NSAIDs.

The four cases we have presented are representative of a cohort of patients on NSAIDs who have developed strictures. Each patient had been taking various NSAIDs in standard doses for variable lengths of time. None of the patients had taken potassium salts. Affected patients presented with either subacute small bowel obstruction or diarrhoea.

The clinical and surgical features in some of these patients were identical with those seen in Crohn's disease. Serosal oedema and hyperaemia were sometimes present, and mesenteric nodes sometimes enlarged. Gross macroscopic appearances ranged from a single, broad-based, fibrous stricture to that of multiple, "diaphragm-like", stenotic lesions that encroached on and narrowed the lumen to a pinhole. Occasionally the lumen was only 1 mm in diameter. At surgery, the affected bowel sometimes appeared macroscopically normal, and the strictures were only detected when an enterotomy was performed. In at least one case (Case 2) inflating the bowel through an enterotomy incision was the best way of detecting the localized narrowings. Pathologically the diaphragm-like strictures showed submucosal fibrosis which was replacing the muscular coat and extending into the lumen in a narrow band-like fold. The strictures usually occurred individually, separated from each other by a small length of normal bowel a few centimetres long. These diaphragm-like strictures appear to represent a new nosological entity (Bjarnason et al, 1988).

There are several important aspects regarding the radiology of these NSAID strictures. Some of the longer strictures may be readily confused with Crohn's disease. However, as far as we are aware the discrete mucosal diaphragms have not been described in Crohn's disease. The diaphragm-like strictures are often undetectable or very difficult to detect by small bowel barium studies because of their localized nature and their resemblance to the plicae circulares.

Because of their relative rarity, the possibility of NSAID-induced intestinal strictures may not be appreciated by some clinicians and radiologists, but should be considered in the differential diagnosis of all patients who have taken NSAIDs and present with malabsorption or small bowel obstruction. Furthermore, a heightened awareness of the possibility of difficult to detect diaphragm-like strictures is important during barium examinations on patients who have been treated with NSAIDs.

References

BJARNASON, I. & PETERS, T. J., 1984. *In vitro* determination of small intestinal permeability. *Gut, 25,* 910–911.

BJARNASON, I., ZANELLI, G., PROUSE, P. *et al,* 1987a. Blood and protein loss via small intestinal inflammations induced by non-steroidal anti-inflammatory drugs. *Lancet, ii,* 711–714.

BJARNASON, I., ZANELLI, G., SMITH, T. *et al,* 1987b. Non-steroidal anti-inflammatory drug induced small intestinal inflammation in humans. *Gastroenterology, 93,* 480–489.

BJARNASON, I., PRICE, A. B., ZANELLI, G. *et al,* 1988. Clinicopathological features of non-steroidal anti-inflammatory drug-induced small intestinal strictures. *Gastroenterology, 94,* 1070–1074.

DAVIES, D. R. & BRIGHTMORE, T., 1970. Idiopathic and drug-induced ulceration of the small intestine. *British Journal of Surgery, 57,* 134–139.

DYER, N. H., KENDALL, M. J. & HAWKINS, C. F., 1971. Malabsorption in rheumatoid arthritis. *Annals of Rheumatic Disease, 30,* 626–630.

KENDALL, M. J. & HAWKINS, C. F., 1971. Xylose test: effect of aspirin and indomethacin. *British Medical Journal, 1,* 533–535.

LONGSTREITH, G. F. & NEWCOMER, A. D., 1975. Drug-induced malabsorption. *Mayo Clinic Proceedings, 50,* 284–293.

MADHOK, R, MACKENZIE, J. A., LEE, F. D. *et al,* 1986. Small bowel ulceration in patients receiving non-steroidal anti-inflammatory drugs for rheumatoid arthritis. *Quarterly Journal of Medicine, 255,* 53–58.

NEOPTOLEMOS, J. P. & LOCKE, T. J., 1983. Recurrent small bowel obstruction associated with phenylbutazone. *British Journal of Surgery, 70,* 244–245.

SAVERYMUTTU, S. H., THOMAS, A., GRUNDY, A. & MAXWELL, J. D., 1986. Ileal stricturing after long term indomethacin treatment. *Postgraduate Medical Journal, 62,* 267–268.

1990, *The British Journal of Radiology*, *63*, 190–196

Salivary gland scintigraphy—a suitable substitute for sialography?

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Abstract. By comparing 27 patients who had both scintigraphy and sialography in the assessment of salivary gland disease, scintigraphy has been shown to correlate well with abnormal sialograms. It is suggested that scintigraphy could become the initial screening procedure in the assessment of salivary gland disease. A normal scintiscan is unlikely to miss significant pathology (as demonstrated by sialography), but sialography must always be performed if there is a suspicion of duct obstruction on scintigraphy. Patients suspected of focal salivary gland pathology such as tumour have not been investigated. The series documents the findings in patients who presented with facial pain, swelling or xerostomia suggesting sialadenitis, duct occlusion or Sjögren's syndrome.

The primary radiological investigation of a salivary gland is sialography. It is invasive and even with excellent technique the appearances bear only a poor relationship to the functional or secretory aspect of the gland. Any changes present are not necessarily recent, and the technique must therefore be viewed with care even in a symptomatic patient. It is rare for sialography to be of "special interest" in a non-specialized centre and is frequently performed by different operators often at junior level. Salivary gland scintigraphy has been available for a number of years and, with a technique using time/activity curves, is an excellent assessment of gland accumulation and secretion in Sjögren's syndrome (Sugihara & Yoshimura, 1988) and "problem" sialograms (Van den Akker & Busemann-Sokole, 1985). It has a lower morbidity than sialography, assesses all four major salivary glands at one sitting, and is not so operator dependent. The authors describe the use of scintigraphy in the assessment of salivary function in 36 patients (27 of whom had sialography also) who presented with a variety of features, mostly salivary gland swelling, pain or xerostomia. Focal pathology is excluded from the series. By comparing sialography and scintigraphy, an evaluation is made whether scintigraphy might offer advantages over sialography as the primary screening procedure.

Materials and methods

Of 36 patients who were examined, all but one were referred from a maxillofacial surgeon (Case 3 was referred from a general physician). Some 42 scans were performed, with six patients scanned twice; 25 were female and 11 male (average age 44 years, range 9–70 years). Most patients were scanned erect with the nose and chin touching the collimator face. In this position 200 MBq ^{99m}Tc pertechnetate was injected intravenously and sequential scintigraphy commenced at the same time. Recently, the dose has been reduced to 100 MBq ^{99m}Tc. Occasionally, patients were scanned supine. Dynamic images were obtained and recorded every minute over a 20 min period. Time/activity curves were recorded on film. The patients remained stationary during this period and at 10 min they were given 10 ml of Carbex solution (Ferring Pharmaceuticals) by mouth through a straw. Carbex is an excellent secretagogue and each 10 ml dose contains 1 g of citric acid. The scintigraphic technique was standard for all the patients, and was not modified according to differing presenting features. Sialography was performed in a standard manner with plain radiographs obtained prior to the cannulation of the appropriate duct and introduction of Lipiodol Ultra-fluid (May and Baker). All but six of the sialograms were performed by one experienced radiologist who has regularly performed six to eight sialograms per month over the last 15 years. Every scintiscan performed since the start of the service (1985) is included in the paper. Sialography preceded scintigraphy in all cases but one (no. 22), and the time interval between the two examinations is given in brackets in Tables II, III and IV. In eight of the 27 patients the two were performed within 20 days of each other, 11 within 40 days, and 20 within 14 weeks. The result of the sialogram was known at the time of reporting the scintiscan, and one observer (different from the sialographer) reported all the scintiscans. The method of reviewing the scintiscan was essentially unchanged throughout the series. The dynamic scan was viewed and the trapping, accumulation and secretion of each of the four main salivary glands assessed. The time/activity curves were correlated with the dynamic scan and in no instance was there marked disagreement between the two sets of data. The final assessment of each of the four glands was based on the curves as presented by Mita et al (1981) (Fig. 1), but not all cases fitted conveniently

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Table I. Scintigraphy alone (nine patients)

	Sex	Age	Presenting features	Scintigraphic findings	Correlation with clinical features
1	Female	44	Xerostomia, xerophthalmia	Normal	Poor
2	Female	70	Xerostomia	Poor accumulation; left parotid gland and left submandibular glands	Fair
3	Female	70	Xerostomia, xerophthalmia	Poor accumulation in three glands	Good
4	Female	15	Prior to removal of submandibular glands for persistent drooling	Poor accumulation in right parotid gland	
5	Female	64	Xerostomia	Poor accumulation in all four glands	Good
6	Female	27	?Block in right submandibular duct	Poor accumulation/secretion in right submandibular gland	Good
7	Female	59	Rheumatoid arthritis, xerophthalmia	Poor accumulation/secretion in both submandibular glands	Fair
8	Female	28	Left parotitis	Poor accumulation in left parotid gland	Good
9	Male	62	Xerostomia, xerophthalmia	Poor accumulation in all four glands	Good

into a particular curve. Patients who attended for a second follow-up scintiscan were noted to have slightly differing curves overall compared with the original, presumably representing a different physiological state at the time of the second scan; for instance a more dehydrated state would result in less production of saliva and a correspondingly poorer trapping accumulation and secretion by all four glands. However, the criteria for determining normality or abnormality was by comparison with the paired gland rather than with any absolute appearance. The dynamic scan excluded artefact due to rotation of the head, by confirming that each of the glands lay equally from the midline structures, and excluded a partially tissued injection by comparing the salivary gland activity with the adjacent thyroid tissue, important in the group I patients in whom a Sjögren's appearance could be simulated by an inadequate blood level of the radiopharmaceutical.

Results

The 36 patients were split into four groups as follows:

1. Scintigraphy alone—nine patients (Table I).
2. 'Failed' sialograms—five patients (Table II).
3. Good correlation between the two techniques in depicting abnormality—nine patients (Table III).
4. Non-correlation between the two techniques in possibly abnormal glands — ten patients (Table IV).

Table II. Failed sialograms (five patients)

	Sex	Age	Presenting features[a]	Scintigraphy
10	Male (two scans)	9	Small ectopic opening on cheek, draining saliva; ?state of right parotid gland (74 days)	All four glands normal; second scan after repositioning of duct: better accumulation pattern but secretion phase poorer
11	Female	50	Right submandibular gland sialadenitis (4 days)	Good accumulation; poor secretion
12	Female	16	Left submandibular gland sialadenitis (4 days)	No accumulation; no secretion
13	Male (two scans)	40	Intermittent obstruction left parotid duct (7 days)	Poor accumulation; no secretion; second scan: no change
14	Female	59	Induration of left submandibular gland area — previous tumour (pleomorphic adenoma) removed in 1975 (2 days)	All four glands normal

[a] Interval between sialogram and scintiscan in brackets.

Table III. Good correlation between scintiscan/sialogram (nine patients)

Sex	Age	Clinical	Scintiscan[a]	Sialogram
15 Male (two scans)	61	Left submandibular gland calculus	Good accumulation; poor secretion (76 days)	Large calculus, sialadenitis; second scan—improvement in secretion following removal of duct calculus
16 Male (two scans)	44	Obstruction left submandibular duct	Good accumulation; poor secretion (40 days)	Dilated duct, calculus; second scan—improvement in secretion following removal of duct calculus
17 Male (two scans, see Fig. 3)	60	Left parotitis	Good accumulation; poor secretion (80 days)	Dilated duct, sialadenitis; second scan—improvement in secretion following removal of duct calculus
18 Female	64	Right submandibular gland sialadenitis	Good accumulation; poor secretion (90 days)	Sialadenitis
19 Female (see Fig. 2)	56	Right parotitis	No accumulation; no secretion (90 days)	Dilated duct, calculus
20 Female	33	Left parotitis	Good accumulation; no secretion (not known)	Sialadenitis
21 Female	13	Left submandibular gland sialadenitis	Poor accumulation; poor secretion (14 days)	Calculus, sialadenitis
22 Male	50	?Block in right submandibular duct	Poor accumulation; good secretion (6 days)	Sialadenitis
23 Male	50	?Block in right submandibular gland	Good accumulation; poor secretion (40 days)	Occluded duct

[a] Interval between scintiscan and sialogram in brackets.

Table IV. Poor correlation between scintiscan and sialogram (ten patients)

Sex	Age	Clinical	Scintiscan[a]	Sialogram
24 Male	33	Right submandibular gland sialadenitis	Normal (4 months)	Dilated duct sialadenitis
25 Female	30	Right parotid gland pain	Normal (11 months)	Dilated duct and intraglandular duct system
26 Female (see Fig. 4)	30	Right parotid gland swelling	Normal right parotid gland; accumulation is normal in other glands also (11 days)	Narrowed duct system and extravasation into gland tissue; ? Sjögren's syndrome
27 Female	40	Right parotitis	Normal (22 days)	Dilated intraglandular ducts, sialadenitis
28 Female	58	Indurated left submandibular gland	Poor accumulation; good secretion (62 days)	Normal
29 Female	35	Left submandibular gland pain	Normal (55 days)	?Duct occlusion; ?technical
30 Female	55	Left submandibular gland sialadenitis	Poor accumulation; good secretion left submandibular gland (80 days)	Normal
31 Female (two scans)	40	Right parotitis	Right parotid gland showed poor secretion; second scan—slight improvement in secretion (7 days)	Normal
32 Female	40	Left parotid gland swelling	Poor accumulation in left parotid gland; poor secretion; ? Sjögrens syndrome (11 months)	Normal
33 Female	30	Right parotitis	Poor accumulation by all four glands; ? Sjögren's syndrome (80 days)	Normal

[a] Interval between scintiscan and sialogram in brackets.

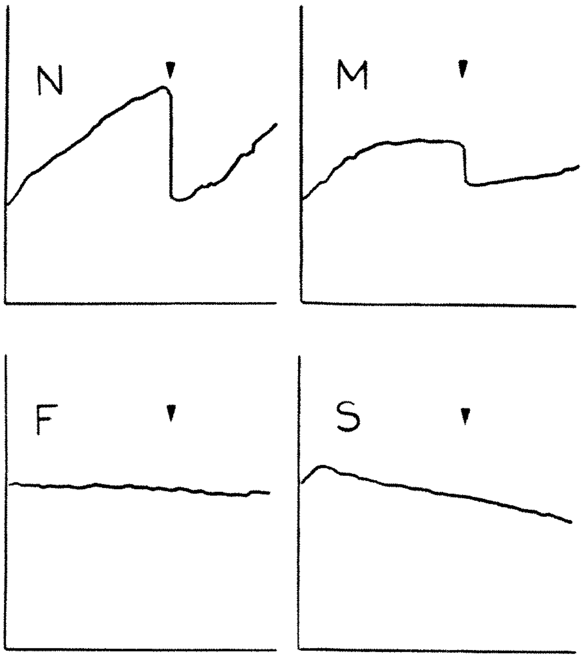


Figure 1. Curve N represents a normal trapping, accumulation and secretion pattern with good response to the secretagogue. Curves M, F and S represent a progressively poorer facility by the gland to trap, accumulate and secrete the radiopharmaceutical. ▼, secretory stimulation.

The three remaining patients had normal scintigraphy and sialography and are not considered further, since the combination of normal scintiscan and sialogram strongly suggests the presenting features are unrelated to salivary gland disease.

Discussion

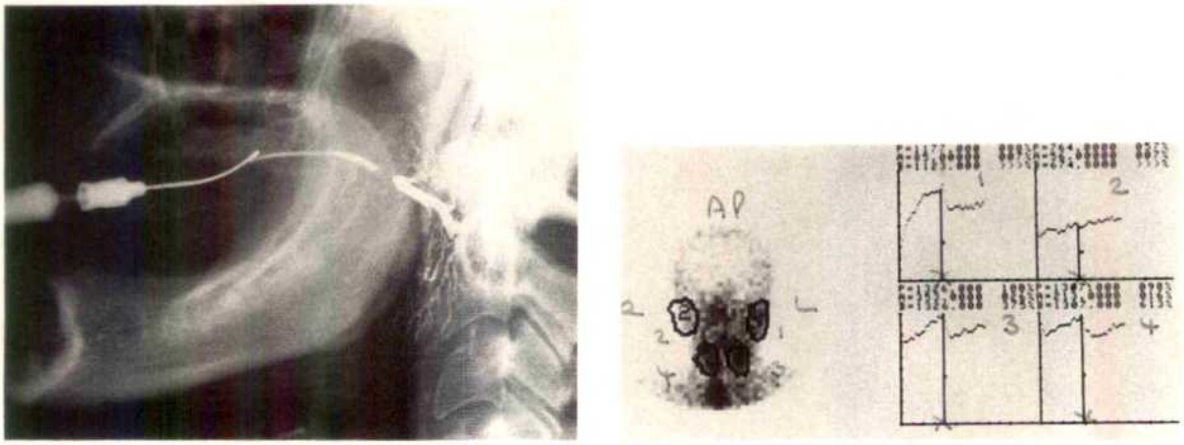
Any comparison between two imaging techniques usually depends upon one of them being a "gold standard" and the other is related to it in a true–positive, true–negative, false–positive, false–negative fashion. Neither sialography nor scintigraphy is the "gold standard", and in fact they indicate different aspects of salivary gland anatomy and function—as indicated by sialographic visualization of the duct system and the accumulation and secretion of a radiopharmaceutical as shown by scintigraphy. However, the issue is not whether one of the studies shows pathology or normality to a degree of accuracy that invalidates the use of the other, but whether scintigraphy should replace sialography as the primary screening technique.

Mishkin (1981) has described the mechanism by which the gland traps, accumulates and secretes the isotope. The intralobular ductule cells have a capacity for trapping and concentrating group VII anions, and these cells concentrate iodine and pertechnetate. These ions, mucus, proteins and enzymes are released as a fluid into the secretory ducts. This is mediated in part by the myoepithelial cells, but it may well be that other factors are also operational in producing the secretory response (Garrett & Emmelin, 1979). It is the lymphocytic periductal infiltrate and duct cell hyperplasia of Sjögren's syndrome that narrows the ducts and produces glandular atrophy with subsequent poor trapping, accumulation and secretion on scintigraphy. The various types of time/activity curve seen in normal and abnormal states are shown in Fig. 1. Basically, the transition from north to south reflects a diminishing functional and secretory capacity by the affected gland (Mita et al, 1981). Scott et al (1984) have demonstrated by animal experimentation that pertechnetate uptake is determined by the mass of acinar rather than solely ductal tissue in the gland, and that scintigraphy is only sensitive to differences exceeding 25% of the gland mass. Sugihara and Yoshimura (1988) mention four cases which showed an F or S type curve and underwent histological examination following removal; all proved to be considerably damaged, suggesting that whatever the cause, if the glandular tissue is destroyed beyond a certain point the time/activity curves tend to F or S type. This article also showed good correlation between sialography and scintigraphy in Sjögren's syndrome and it seems unnecessary to perform sialography on a patient suspected of Sjögren's syndrome in whom the scintiscan demonstrates a typical F or S type curve affecting two or more glands.

Nine patients in the series had scintigraphy alone without sialography, and Table I assesses the correlation between clinical and scintigraphic findings. Six of the nine patients were referred with features suggesting Sjögren's syndrome, usually xerostomia, of whom three had good scintigraphic correlation and two had fair. Not all patients with xerostomia have Sjögren's syndrome and some patients with only mild xerostomic salivary disturbance have markedly abnormal scintigraphic studies, indicating the sensitivity of the technique (Fox et al, 1985). A number of patients in the present series had abnormal scintigraphy of clinically asymptomatic glands, possibly indicating subclinical Sjögren's syndrome (Case 33).

Two cases in Table I had a symptomatic single gland problem. Scintigraphy correlated well with the clinical findings in both patients. The final case in this group demonstrates the use of scintigraphy to assess the functional status of the parotid glands prior to removal of the submandibular glands in a patient with cerebral palsy who had persistent drooling despite redirecting the parotid ducts. This functional information can only be provided easily and accurately by scintigraphy.

Five of the 27 patients in whom it was attempted had unsuccessful sialography, with a failure to cannulate the duct or inadequate filling. This usually indicates duct pathology, and in three patients abnormal scintigraphy confirmed this with poor or no secretion of the isotope. However, another patient had a normal scintiscan, suggesting that the failure to perform a sialogram was purely technical. A 9-year-old boy with an ectopic duct orifice opening onto his cheek was examined by scintigraphy pre- and post-repositioning of the parotid duct



(a)

(b)

Figure 2. *Case 19*, see Table III. (a) The right parotid sialogram demonstrates a duct calculus with marked proximal dilatation of the intraglandular duct segments. (b) The corresponding scintiscan curve (2) reveals no trapping, accumulation or secretion of the isotope, indicating a severely damaged gland (F type curve).

opening. Sialography via the ectopic duct orifice was unsuccessful owing to a poor seal at the opening on the cheek. This group of five patients accounted for 18% of all the sialograms attempted and without scintigraphy no functional or secretory information of the glands would have been obtained.

All the patients in Table III had an abnormal sialogram with a calculus and/or sialadenitis with or without duct occlusion. All the patients with occluded ducts had an abnormal scintiscan, mostly in the secretion phase, but only two had accumulation impairment. Scintigraphy detected all duct occlusions and gave valuable information regarding function (Figs 2 and 3). If the gland is poorly functioning or non-functioning on scintigraphy and is a source of infection the surgeon may decide to remove it. Six patients had sialadenitis demonstrated on sialography of whom three had a duct occlusion problem. On scintigraphy four had a good accumulation phase but only one had a good secretion phase. Previous papers have shown that sialadenitis produces an increase in the accumulation phase (van den Akker and Busemann-Sokole, 1985), but this is not confirmed in the present series. Perhaps our relatively short accumulation phase of 10 min has not allowed this increase to take place. Possibly the poor secretory response in these glands reflects damage to those elements which mediate normal secretion of saliva. A longer accumulation phase might provide more information, but it seems unreasonable to expect a patient to remain stationary against the collimator face for more than 20 min. A Cephalostat type of stabilizing device might prove useful to immobilize the head, but there was no instance of a failed scintiscan resulting from patient movement in the present series.

The final group of 10 patients in Table IV is the most difficult to assess. Any direct comparison between scintigraphy and sialography in a symptomatic gland is scarcely valid since each test provides different information. If scintigraphy does not miss any significant pathology (as shown on sialography) and adds further information, then it should be considered as the primary screening procedure since it has a lower morbidity than sialography and will provide functional and secretory information on all four glands. The ten patients in this group have the longest interval between scintigraphy and sialography compared with other groups, and this might account for some discrepancy. However, salivary gland disease is unlikely to alter markedly, once established. Since scintigraphy correlated well with the sialographic changes of duct occlusion in Table III, the normal scintiscan in Case 29 is considered to be the true normal. Clinical follow-up over a year has failed to detect any developing submandibular gland pathology. Cases 24 and 27 represent false-negative scintigraphy. Both patients had a clinical history suggesting sialadenitis, confirmed on sialography. However, scintigraphy showed a normal trapping and accumulation pattern but confirmed the absence of any duct obstruction. Case 25 is considered a false-positive sialogram. The patient's facial pain resolved following treatment with a bite-raising appliance, suggesting a temporomandibular joint problem. Case 26 is difficult to assess. Clinical follow-up was not possible as the patient left the district shortly after the two examinations, but the normal scintigraphy probably excludes a diagnosis of Sjögren's syndrome, and the sialography is considered to be falsely positive.

The remaining five cases in this group all had abnormal scintigraphy and normal sialography. Case 31 has been followed up in clinic for 16 months, and is considered to have had falsely negative sialography. She has continued to have episodes of parotitis with probable iritis. However, diagnostic tests for Sjögren's syndrome were all negative. Case 28 was found at

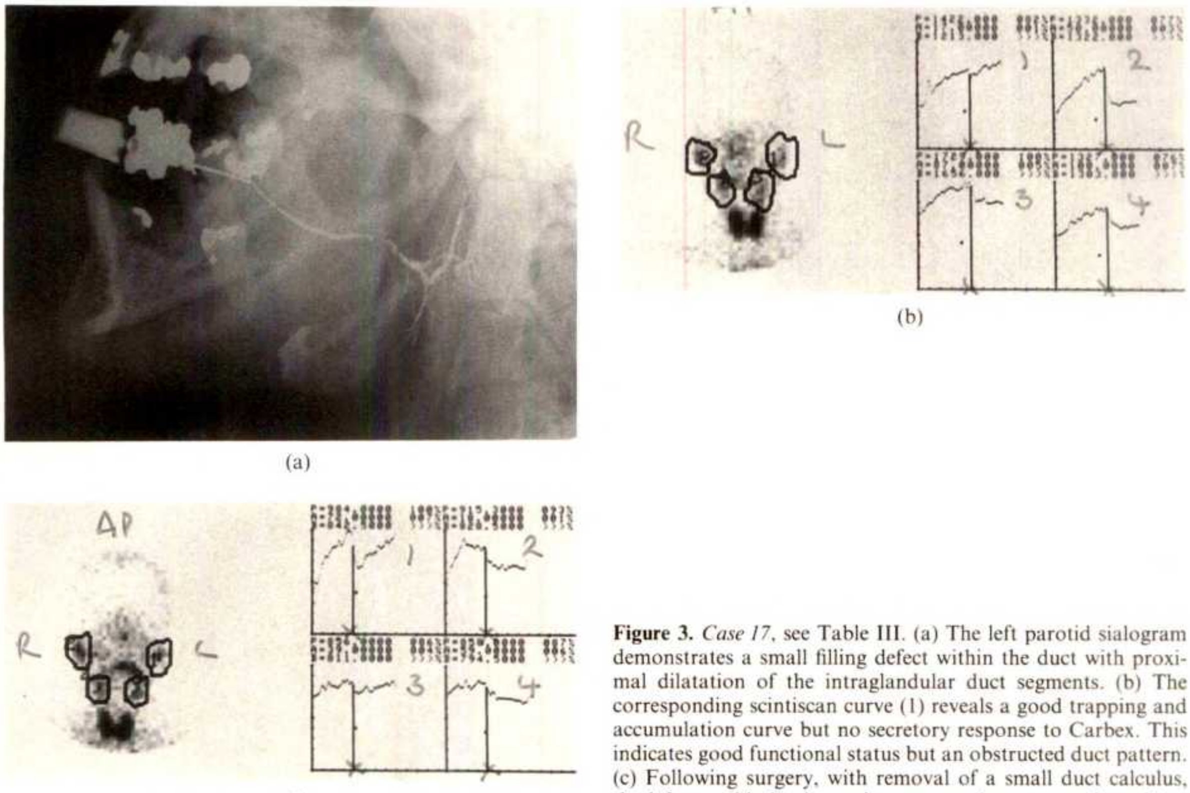


Figure 3. *Case 17*, see Table III. (a) The left parotid sialogram demonstrates a small filling defect within the duct with proximal dilatation of the intraglandular duct segments. (b) The corresponding scintiscan curve (1) reveals a good trapping and accumulation curve but no secretory response to Carbex. This indicates good functional status but an obstructed duct pattern. (c) Following surgery, with removal of a small duct calculus, the left parotid gland now has a normal secretory phase (1).

surgery to have an enlarged lymph node compressing the left submandibular gland (histologically showed sarcoid), but the underlying submandibular gland was considered normal. Scintigraphy therefore is considered to be falsely positive, although the compression by the enlarged node may have contributed to the poor function. Case 32 has an 11 month interval between the two tests, but since a labial gland biopsy and progressive xerophthalmia confirmed the diagnosis of Sjögren's syndrome, scintigraphy is regarded as the true–positive

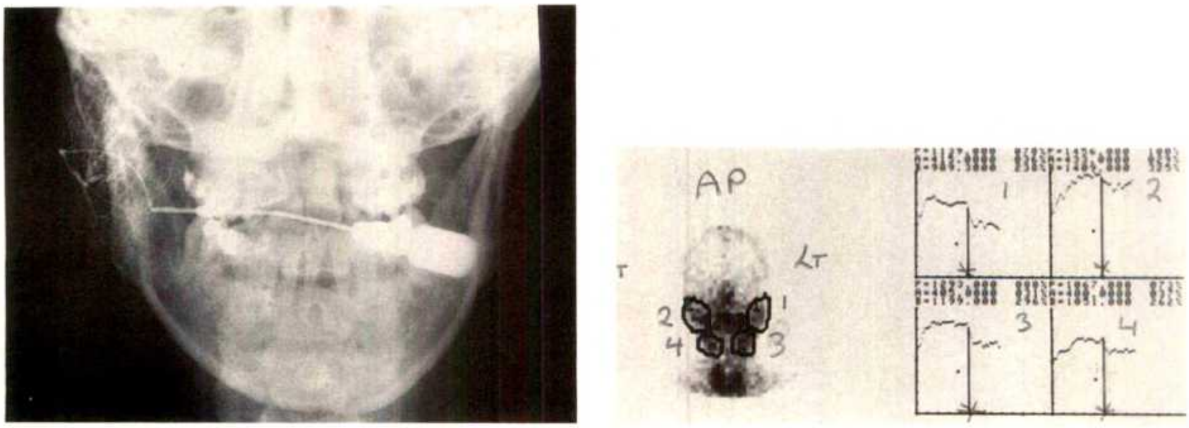


Figure 4. *Case 26*, see Table IV. (a) The right parotid sialogram reveals a narrowed duct system with minimal extravasation of contrast medium into gland tissue: ?Sjögren's syndrome. (b) The corresponding scintiscan curve (2) indicates good trapping, accumulation and secretion by the gland. The sialographic appearances are therefore falsely positive for Sjögren's syndrome.

examination. Case 33 was followed for 6 months with clinical improvement. She was discharged without any definite diagnosis, although tests for Sjögren's syndrome were not performed. The clinical history of Case 30 suggested sialadenitis, and the scintiscan demonstrated a degree of functional impairment despite a normal sialogram. No definite diagnosis was reached.

Discussion–summary

The article presents data on 36 patients with features of salivary gland disease who had salivary gland scintigraphy; 27 of the 36 patients also had sialography of the symptomatic gland. In five patients, sialography was technically unsatisfactory. In the majority of cases there was good agreement between scintigraphy, sialography and clinical findings. All duct occlusion problems were accurately detected by scintigraphy, and follow-up scans in three patients demonstrated improvement in the secretory pattern following removal of the duct obstruction. In ten cases there was poor correlation between scintigraphy and sialography.

Scintigraphy is an accurate test of the function and secretion of salivary glands and should be considered as a substitute for sialography in the assessment of possible sialadenitis, duct occlusion or Sjögren's syndrome.

Acknowledgments

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References

Fox, P. C., Van der Ven, P. F., Sonies, B. C., Weiffenbach, J. M. & Baum, B. J., 1985. Xerostomia: evaluation of a symptom with increasing significance. *Journal of the American Dental Association, 110,* 519–525.

Garrett, J. R. & Emmelin, N., 1979. Activities of salivary myoepithelial cells. *Medical Biology, 57,* 1–28.

Mishkin, F. S., 1981. Radionuclide salivary gland imaging. *Seminars in Nuclear Medicine, 11,* 258–265.

Mita, S., Kohono, M., Matuoka, Y. & Irimajiri, S., 1981. Diagnostic availability of RI—sialography in Sjögren's syndrome. *The Ryumachi, 11,* 305–316.

Scott, J., Cawood, J. I., Grime, J. S., Critchley, M. & Jones, R. S., 1984. Histological evaluation of quantitative scintigraphy of the salivary glands in a primate model. *International Journal of Oral Surgery, 13,* 45–52.

Sugihara, T. & Yoshimura, Y., 1988. Scintigraphic evaluation of the salivary glands in patients with Sjögren's syndrome. *International Journal of Oral Maxillofacial Surgery, 17,* 71–75.

Van den Akker, H. P. & Busemann-Sokole, E., 1985. Absolute indications for salivary gland scintigraphy with ^{99m}Tc pertechnetate. *Oral Surgery, 60,* 440–447.

1990, *The British Journal of Radiology*, *63*, 197–201

Superselective embolization using a coaxial catheter technique

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Abstract. A method of superselective embolization of 0.64 mm or 0.89 mm coils using a coaxial catheter system is described. The normally functioning parts of an organ can be easily preserved. A number of clinical cases are briefly described which illustrate the application of this method. It is particularly suited to the control of bleeding points in diseased organs or precious organs such as transplants where embolization of a larger volume of tissue would have serious consequences.

The technique and the role of therapeutic arterial embolization are well established in many clinical situations (Allison, 1986). The management of arterial bleeding from specific branch vessels demands a more selective approach than the embolization of tumour within organs such as the liver or the kidney.

Selective embolization may be accomplished by several methods including the use of detachable balloons and positioning coils on Marsmann wires. We describe the use of a coaxial catheter system (Waltman, 1982) for superselective embolization of 0.64 mm and 0.89 mm coils of a small vascular territory.

Technique

A complete arteriogram is performed to provide full vascular mapping. The arterial (or venous) branch to be occluded is selected from the diagnostic arteriogram. The diagnostic catheter (7 or 8 French depending on which diameter coil is used) is advanced selectively into the main feeding vessel. A sidewinder, cobra or other femorovisceral catheter is used as required. This is the guide for the coil delivery system.

To place an 0.64 mm coil a 3 French Teflon infusion catheter (William Cook) is used via a 7 French guide catheter. The 3 French catheter preloaded with an 0.45 mm high-torque floppy guide-wire (ACS) is fed coaxially through a Tuohy–Borst adaptor. The guide-wire is advanced subselectively to the chosen position (Meyerovitz et al, 1985) and the small catheter is fed over it. Injection of dilute contrast medium confirms the catheter tip position after the wire has been withdrawn. The 3 French catheter is not visible fluoroscopically unless contrast is injected or the wire is inside it. After contrast injections, saline flushing is necessary to prevent the coil sticking within the catheter during delivery.

An 0.64 mm embolization coil 2.5 or 5 cm long (William Cook) is pushed through the central 3 French catheter by a stiff 0.64 mm guide-wire (ACS) exactly 2 cm longer than the catheter. The coil is therefore completely delivered when the last 2 cm of guide-wire protrude from the coaxial catheter. The coil must not be pushed beyond the chosen site. The pushing wire must be sufficiently stiff to extrude the coil completely. In cases where the catheter system makes a tight bend the 2.5 cm coils are subjectively easier to push around the curve than the longer coils. Further coils are then delivered as required.

The 0.89 mm coils may be placed similarly through a 4 French coaxial catheter (Radiologic) via an 8 French guide catheter using an 0.89 mm guide-wire as pusher.

It may take 10–15 min for clot to form on the coils and achieve vessel occlusion. However, if occlusion of the vessel is not demonstrated by contrast examination after placing the coils a small quantity of material such as Sterispon or autologous blood-clot can be injected via the coaxial catheter. These and other embolic materials can be injected through a 4 French system but there is some difficulty administering Sterispon through a 3 French catheter.

Case reports

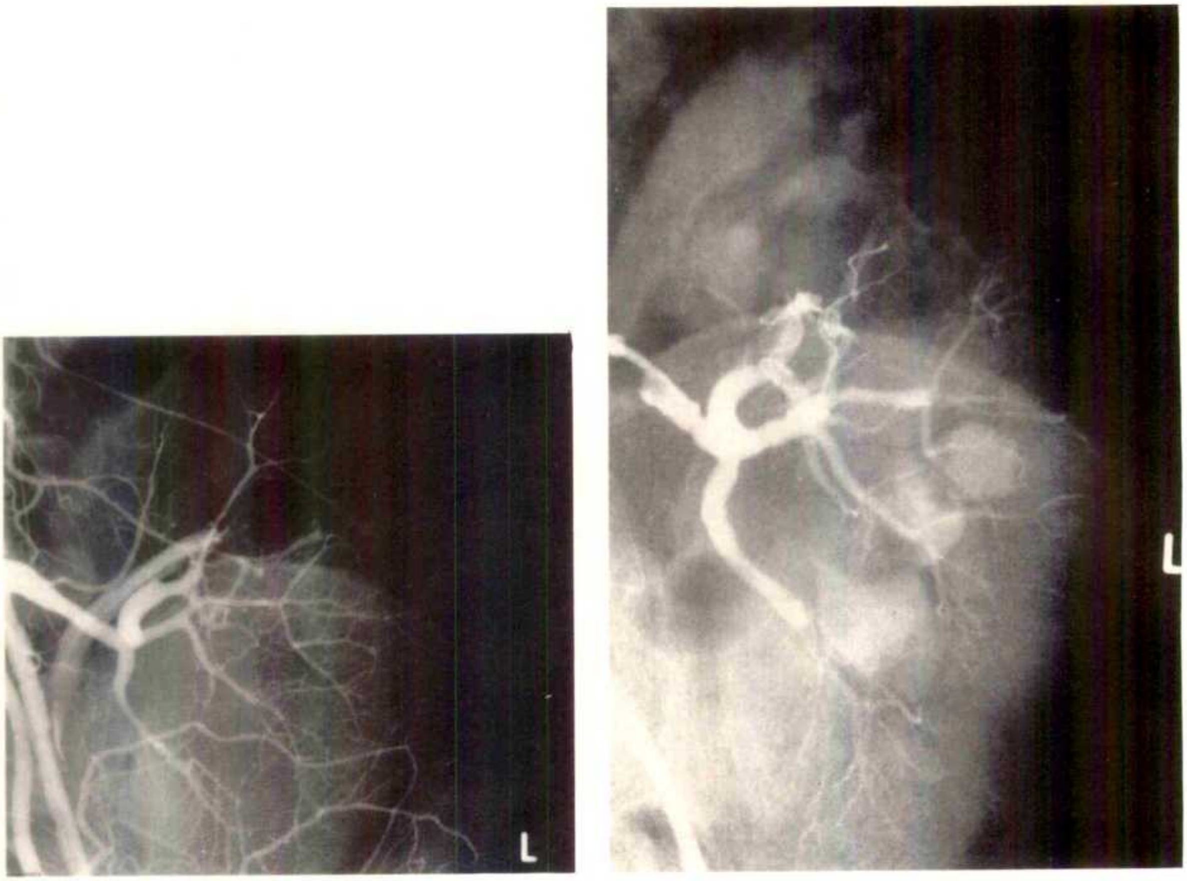
The following cases illustrate the use of the system.

Cases 1–3

Selective coil embolization of bleeding points following renal biopsy controlled haematuria in three patients—two with transplant kidneys (Fig. 1) and one native kidney (Fig. 2). Bleeding was of sufficient severity to require transfusion in all three cases and surgery was avoided by embolization. One patient required a repeat procedure to complete control from a separate bleeding biopsy site.

Case 4

One patient bleeding from a bladder tumour was treated by embolization of a vesical branch of the internal iliac artery.



(a) (b)

Figure 1. (a) Left iliac arteriogram showing transplant kidney with arteriovenous fistula. The patient had severe haematuria following a biopsy. (b) After selective embolization of coils the fistula is closed. Haematuria was controlled. Although a significant proportion of the upper pole vasculature is occluded the renal function was preserved.

Case 5

A patient with Budd–Chiari syndrome developed haemobilia and a right hepatic bruit following liver biopsy. Arteriography showed an arterioportal and arteriocollateral venous fistula supplied by a branch of the right hepatic artery arising from the superior mesenteric artery (Fig. 3). Superselective deposition of 0.64 mm coils occluded the fistulae and stopped the haemobilia.

Case 6

Similar fistulae were demonstrated and embolized in a man with primary sclerosing cholangitis who was noted to have a palpable thrill at the site of previous liver biopsies (Fig. 4). He also had a large replaced right hepatic artery. After embolization the thrill was no longer palpable.

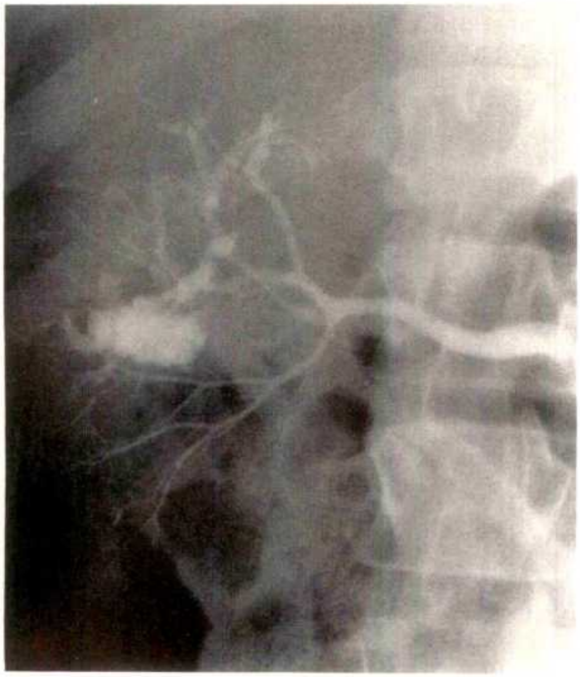
Case 7

A bleeding branch of the right hepatic artery was selectively occluded in a young man stabbed through the liver and right lung. This successful embolization was considered to be have reduced the blood loss and aided the surgeon at subsequent laparotomy to suture other bleeding sites.

Discussion

Although coaxial catheter techniques are well recognized (Young et al, 1988) we believe this is the first

Figure 2. (a) Right renal arteriogram showing a central blush of contrast at the site of renal biopsy. There is also an arteriovenous fistula in the upper pole. (b) One second later there is rapid flow of contrast down the ureter. This patient had very severe haematuria. (c) Several coils have now been placed selectively through the 4 French catheter. The guide catheter can be seen with its tip in the origin of the renal artery. (d) Arteriogram after withdrawal of coaxial 4 French catheter shows no further central leakage of contrast. There is a small arteriovenous fistula in the upper pole. After this the haematuria resolved.



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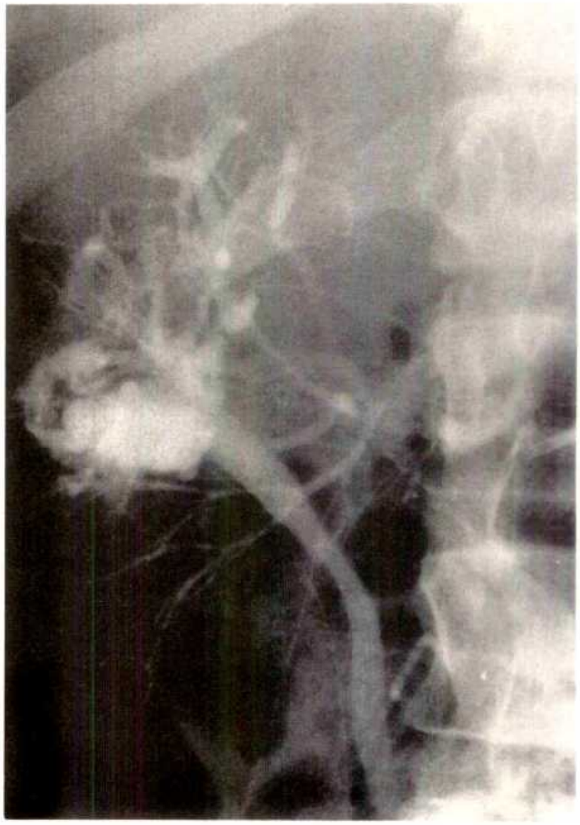

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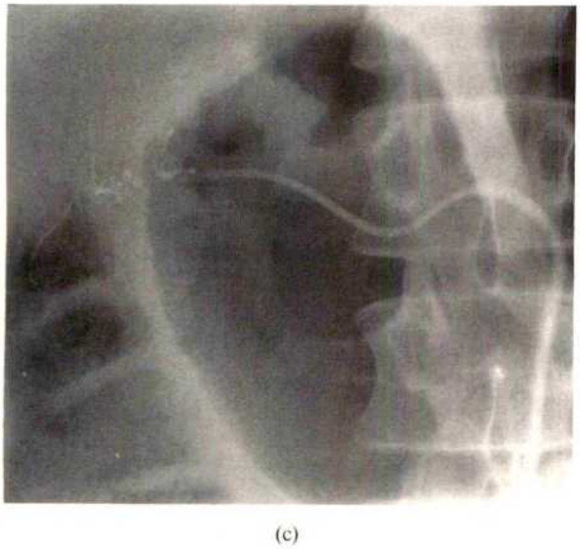

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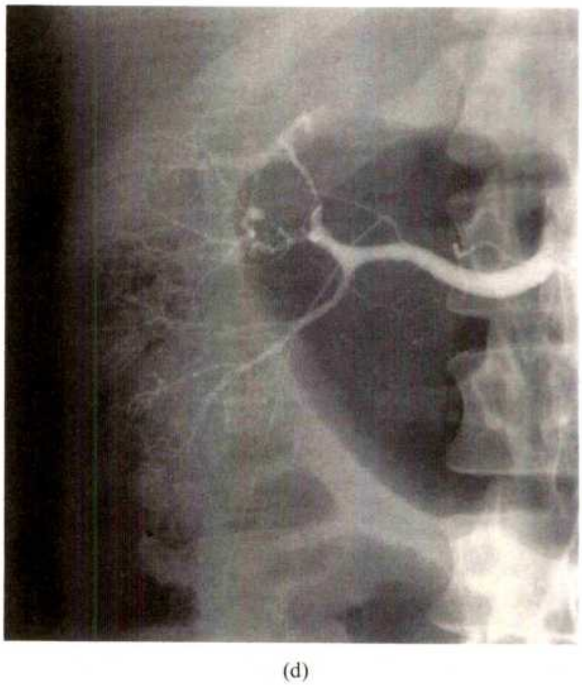

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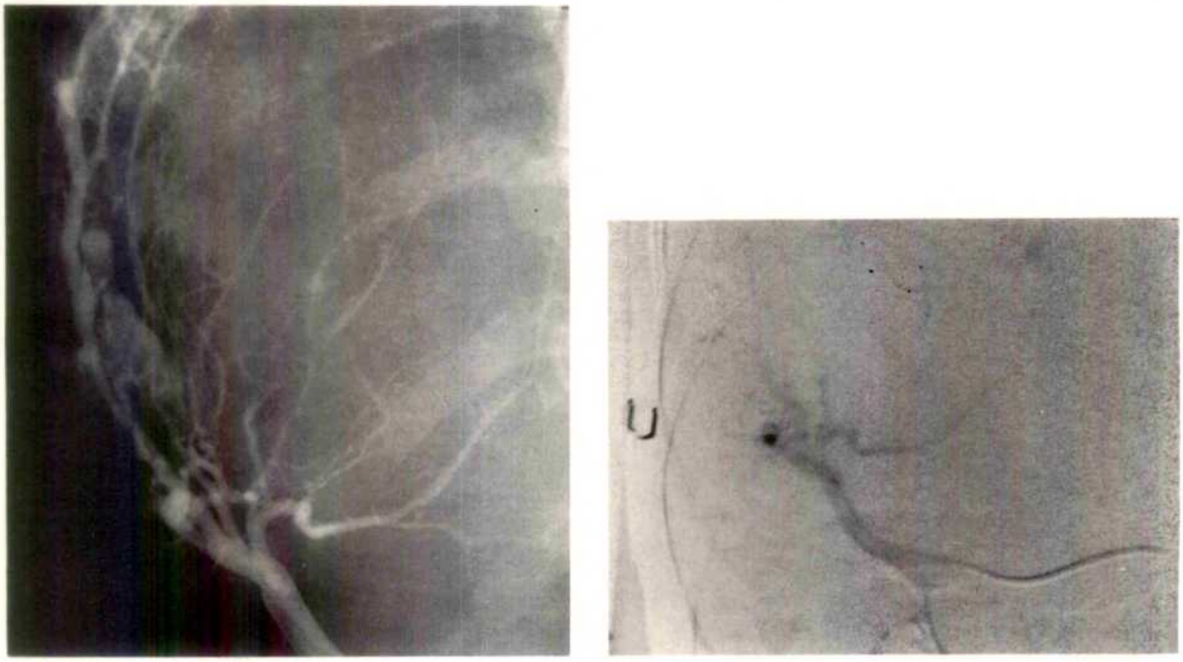
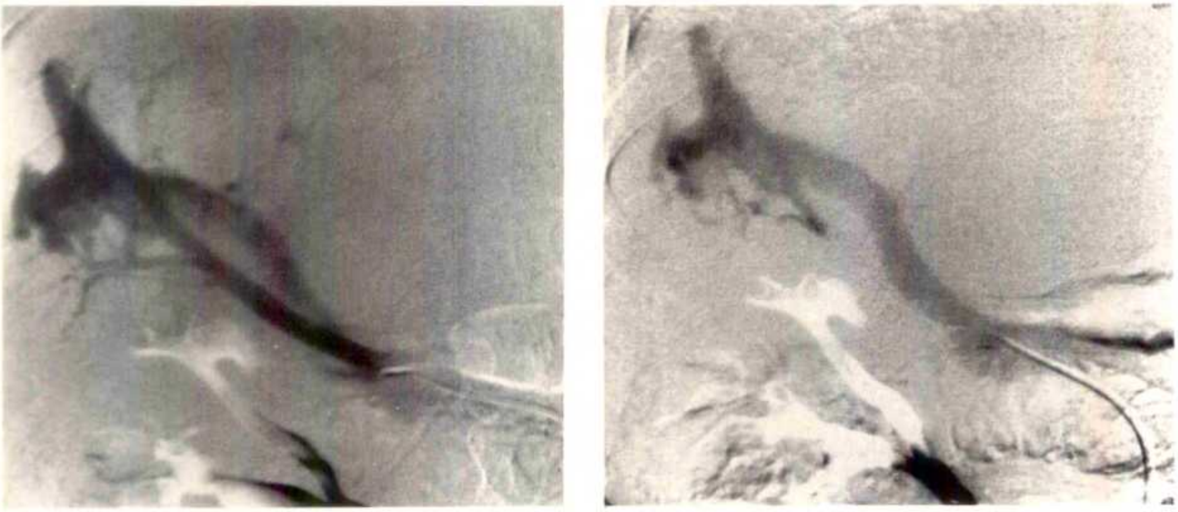


(a) (b)

Figure 3. (a) Selective right hepatic arteriogram showing contrast flowing into a superficial venous collateral and a dilated right branch of the portal vein. The hepatic arterial branches are all stretched around the enlarged caudate lobe. The patient suffered melaena caused by haemobilia after a liver biopsy performed for Budd–Chiari syndrome. (b) Digital subtraction angiogram following embolization and withdrawal of the 3 French catheter. There is now no flow through the fistulae into the portal vein or superficial collateral vein. The melaena resolved.



(a) (b)

Figure 4. (a) Digital subtraction right hepatic arteriogram showing a high flow of contrast through a fistula into the portal vein and demonstrating retrograde flow within the portal vein. This patient was noted to have a thrill at the site of previous liver biopsies. (b) Selective digital subtraction arteriogram performed through the 3 French catheter which has been advanced to the branch to be occluded by embolization coils. The fine 3 French catheter can just be seen. After embolization the thrill had disappeared.

report of the use of this system with 0.89 mm coils, although these coils may also be used for embolization through a standard tapered diagnostic catheter. This technique permits easy superselective embolization following catheterization with the coaxial catheter fed over the high-torque guide-wire. The risk of intimal damage may be less than with subselective catheterization by a standard catheter. Coil placement is relatively quick which enables control of active bleeding sites. Severe haemorrhage from renal biopsy sites was controlled within approximately 1 hr total procedure time with the 8 French/4 French system and 0.89 mm coils. Nephrectomy was thus avoided.

The technique is ideal for treating very specific focal lesions such as bleeding points from biopsy or other penetrating trauma. More of the internal vasculature of an organ is spared than with conventional embolization methods. This is important in preserving liver cell or renal function especially in an already diseased or a precious organ such as a transplant.

The technique enables embolization of specific regions supplied by very small vessels with no risk to adjacent areas. This is important in the pelvis where internal iliac embolization carries a risk of sciatic nerve damage (McIvor et al, 1982; Hare & Holland, 1983).

As the coils open out on extrusion from the coaxial catheter there is no risk of migration unless they are released within a large vessel or they are pushed more distally by the wire or catheter. Careful selection of the site, choice of coil and meticulous technique avoids these problems. Ideally the coils form 'coils' within the artery on extrusion to allow maximal clot formation. In patients with renal artery vasoconstriction due to hypotension the coils may remain elongated which might reduce the effective occlusion (see Fig. 1b) or occlude a larger proportion of the renal circulation than intended.

References

Allison, D. J., 1986. In *Diagnostic Radiology*, ed. by R. G. Grainger & D. J. Allison (Churchill Livingstone, Edinburgh) pp. 2146–2158.

Hare, W. S. & Holland, C. J., 1983. Paresis following internal iliac artery embolization. *Radiology*, *146*, 47–51.

McIvor, J., Williams, G. & Southcott, R. D. G., 1982. Control of severe vesical haemorrhage by therapeutic embolisation. *Clinical Radiology*, *33*, 561–568.

Meyerovitz, M. F., Levin, D. C. & Boxt, L. M., 1985. Superselective catheterization of small-caliber arteries with a new high-visibility steerable guide wire. *American Journal of Roentgenology*, *144*, 785–786.

Waltman, A. C., 1982. Catheter systems used in therapeutic angiography and methods of superselective vessel catheterization. In *Interventional Radiology*, ed. by C. A. Athanasoulis, R. C. Pfister, R. E. Greene & G. H. Roberson (Saunders, Philadelphia) pp. 14–21.

Young, A., Tadavarthy, S. M., Coleman, C. C., Lund, G., Hunter, D. W., Cragg, A. H., Cardella, J. F., Darcy, M. D., Smith, T. P., Castaneda, F., Amplatz, K. & Castaneda-Zuniga, W. W., 1988. Embolotherapy: agents, equipment and techniques. In *Interventional Radiology* ed. by W. R. Castaneda-Zuniga & S. M. Tadavarthy, (Williams and Wilkins, Baltimore) pp. 36–37.

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Nasopharyngeal carcinoma: pattern of skeletal metastases

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Abstract. The records of 153 nasopharyngeal carcinoma patients with skeletal metastases were reviewed. The skeletal system was the most common site of distant metastases. The patients who developed skeletal metastases were significantly younger than those without skeletal metastases, although there was no difference between sexes. The pattern of skeletal involvement conforms to the general pattern, the spine and pelvis being the common sites. The first region of involvement was lumbar spine (28.4%), then dorsal spine (27.7%), sacrum and pelvis (16.3%), femur (9.9%), rib and sternum (7.8%), humerus (5.0%), cervical spine (3.5%) and skull vault (1.4%). Radiologically, the lesions were lytic in 66.0%, mixed lytic and sclerotic in 12.8% and sclerotic in 21.2%. The time to development of symptomatic skeletal metastases of mixed or sclerotic nature was significantly longer than lytic lesions, and patients with mixed or sclerotic metastases also had better survival.

Compared with other head and neck tumours, nasopharyngeal carcinoma has a higher incidence of distant metastases (O'Brien et al, 1971; Probert et al, 1974; Merino et al, 1977). Based on clinical information without autopsy, 14.9–40.5% of distant metastases have been reported for nasopharyngeal carcinoma (Perez et al, 1969; Thompson et al, 1970; Moench et al, 1972; Hoppe et al, 1976; Bedwinek et al, 1980; Mesic et al, 1981), compared with 5.3–23.6% reported for other head and neck cancers (Castigliano et al, 1954; Arons et al, 1961; Hoye et al, 1962; Rubenfeld et al, 1962; Berger & Fletcher, 1971; Probert et al, 1974; Merino et al, 1977). While the other head and neck cancers involved the lungs as the most common site of distant metastases, the most common distant failure site for nasopharyngeal carcinoma was bone (Moench et al, 1972; Hoppe et al, 1976; Merino et al, 1977; Mesic et al, 1981; Sham et al, 1990). Huang (1980) reported axial skeleton and the long bones as the most common sites of involvement, but there has been no detailed description of the nature of bone metastases from nasopharyngeal carcinoma in the English literature.

We have reviewed the records of 153 patients with nasopharyngeal carcinoma who developed skeletal metastases with emphasis on the pattern of involvement, radiological features and the impact of skeletal metastases on survival.

Patients and methods

From January 1976 to December 1983, 841 patients with newly diagnosed nasopharyngeal carcinoma were referred to our department. Of these, 45 either refused treatment or died before the completion of radiotherapy from advanced disease; another 37 had distant metastases (Stage V disease) at presentation. These 82 patients were excluded from the present study. Of the remaining 759 Stage I to IV patients, 153 developed skeletal metastases after the completion of treatment, and they formed the basis of the present analysis.

Details of patient characteristics, staging procedures and treatment of this group of 759 patients have been reported previously (Sham & Choy, 1990). After completion of radical radiotherapy all patients were followed up every 4–6 weeks for the first year, every 2 months for the second year, every 3 months for the third year and then half-yearly. At each visit the nasopharynx, the neck and the abdomen were carefully examined. Chest radiograph was performed yearly. When skeletal metastasis was suspected because of bone pain, plain radiographs of the appropriate region of skeleton were obtained. When the pain was persistent, or when the clinical suspicion was high but the radiographs were not conclusive, bone scintigraphy was performed.

For analysis of the pattern of involvement, the skeletal system was divided into eight regions: cervical spine, lumbar spine, dorsal spine, sacrum and pelvis, femur, humerus, rib and sternum, and skull vault (excluding base of skull involvement by direct extension). A region was said to be involved if there was pain corresponding to radiological evidence of skeletal metastases. Metastases that brought about the destruction of bone were designated as osteolytic and metastases that brought about new bone formation were designated as osteoblastic. When both destruction and proliferation areas were present, the metastases were designated as mixed type. Patients with skeletal metastases shown by bone scintigraphy were excluded from the analysis on the pattern of involvement because the sensitivity of bone scintigraphy often reveals multiple

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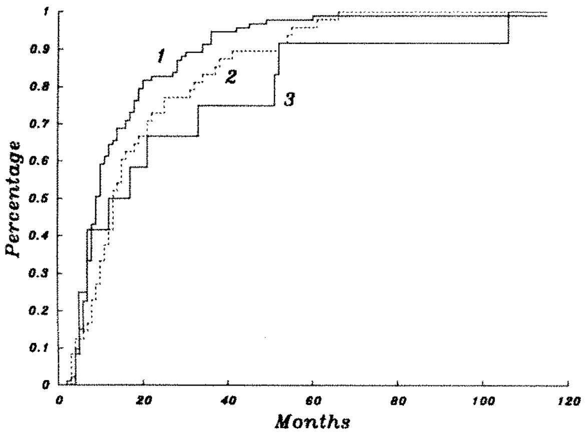

Figure 1. Time to manifestation of skeletal metastases: 1, patients with lytic bone metastases; 2, patients with mixed or sclerotic bone metastases; 3, patients with skeletal metastases diagnosed by bone scintigraphy ($p=0.04$ for groups 1 and 2, $p=0.13$ for groups 1 and 3, $p=0.48$ for groups 2 and 3).

involvement before some of the lesions become symptomatic.

The time to development of skeletal metastasis, the actuarial risk of developing a symptomatic lesion in another skeletal region and the actuarial survival, starting from the date of diagnosing skeletal metastases, were computed by the Kaplan–Meier method and the difference between curves tested by the Mantel–Cox test (Kaplan & Meier, 1958; Mantel & Haenszel, 1959). Computations were performed by the 1L module of the BMDP Statistical Software.

Results

Out of the 759 patients, 276 (36.4%) patients developed distant metastases in one or more organ-systems: 153 patients developed skeletal metastases, 102 developed lung metastases, and 72 developed liver metastases.

Of the 153 patients with skeletal metastases, there were 119 males (77.8%) and 34 females (22.2%). Their age ranged from 18 to 78 years, with median age of 45.9 years.

These 153 patients had significantly more advanced stage than the 606 patients who had no diagnosed skeletal metastases ($p<0.0001$, by Mann Whitney U-test).

There was no significant difference in sex distribution between the 153 patients with skeletal metastases and the 606 patients without. The group of patients with skeletal metastases however was significantly younger than group without (median age of 45.9 years and 49.0 years respectively, $p=0.006$, by Student's t-test).

Pain was the main presenting symptom in all patients. The diagnosis of bone metastases was by radiographs in 141 patients and bone scintigraphy in the remaining 12 patients. These 12 patients had persistent bone pain but repeated radiographs were normal while bone scintigraphy showed multiple areas of increased uptake in the skeleton, with one or more areas corresponding to the symptomatic sites.

For the 141 patients with radiographic evidence of bone metastases, the lesions were lytic in 93 (66.0%), mixed lytic and sclerotic in 18 (12.8%) and sclerotic in 30 (21.2%).

The time to development of symptomatic skeletal metastases from diagnosis of nasopharyngeal carcinoma ranged from 2 months to 113 months, the median time being 9.5 months. Eighty per cent of skeletal metastases were manifested by 24 months. The time to development of symptomatic skeletal metastases of mixed or sclerotic nature was significantly longer than lytic lesions ($p=0.04$, Fig. 1).

The first and second skeletal region with symptomatic metastases in the 141 patients with radiological evidence are shown in Table I. The first skeletal region in descending order of frequency was lumbar spine, 40 patients (28.4%); dorsal spine, 39 (27.7%); sacrum and pelvis, 23 (16.3%); femur, 14 (9.9%); rib and sternum, 11 (7.8%); humerus, 7 (5.0%); cervical spine, 5 (3.5%) and skull vault (excluding base of skull involvement by direct extension), 2 (1.4%).

The actuarial risk of developing symptomatic metas-

Table I. First and second skeletal region with symptomatic metastases, and the total number of patients who developed symptomatic metastases in each skeletal region

Region	Number of patients with this region involved as first site	Number of patients with this region involved as second site	Total number of patients with this region involved in the course of disease
Cervical spine	5 (3.5%)	0 (0.0%)	7 (5.0%)
Dorsal spine	39 (27.7%)	18 (12.8%)	67 (47.5%)
Lumbar spine	40 (28.4%)	29 (20.6%)	80 (56.7%)
Sacrum-pelvis	23 (16.3%)	17 (12.1%)	56 (39.7%)
Humerus	7 (5.0%)	3 (2.1%)	13 (9.2%)
Femur	14 (9.9%)	7 (5.0%)	32 (22.7%)
Rib-sternum	11 (7.8%)	4 (2.8%)	27 (19.1%)
Skull vault	2 (1.4%)	2 (1.4%)	5 (3.5%)
Total number of patients	141	80	141

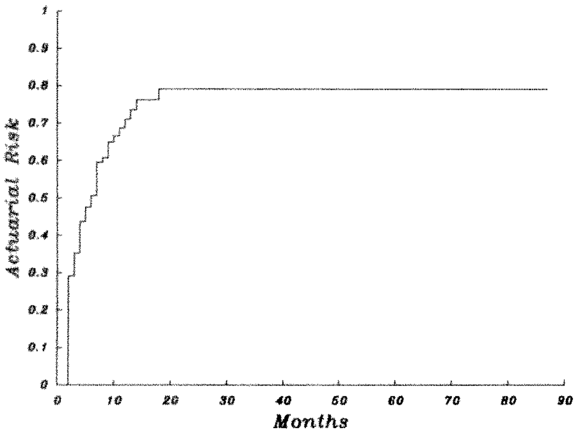

Figure 2. Actuarial risk of developing symptomatic lesion in another skeletal region (for patients with lytic, mixed or sclerotic lesions).

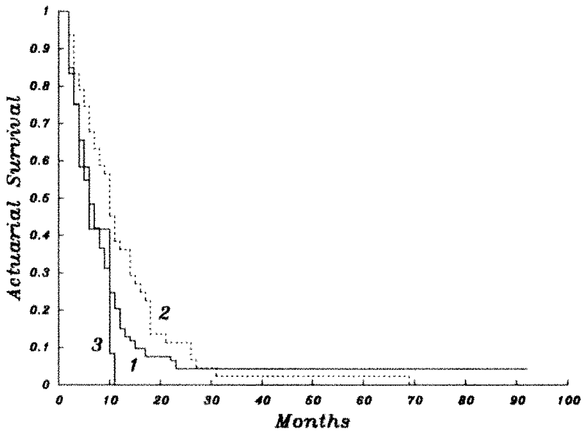

Figure 3. Actuarial survival after diagnosis of skeletal metastases: 1, patients with lytic bone metastases; 2, patients with mixed or sclerotic bone metastases; 3, patients with skeletal metastases diagnosed by bone scintigraphy ($p=0.03$ for groups 1 and 2, $p=0.32$ for groups 1 and 3, $p=0.005$ for groups 2 and 3).

tases in another region is shown in Fig. 2. Patients who died before the development of symptomatic lesion in another skeletal region were considered censored. Twenty-four patients (17%) had simultaneous symptomatic lesions in more than one region at the first documentation of skeletal metastases. By 5.5 months, 50% of patients had developed symptomatic lesions in another skeletal region. There was no statistical difference in this aspect of metastases between patients with different radiological patterns of involvement ($p=0.42$). More than half the patients developed symptomatic metastatic lesions in two or more skeletal regions before death or the last follow-up (Table II). The total number of patients who developed symptomatic lesions in each skeletal region is shown in Table I.

The actuarial survival starting from the date of diagnosis of skeletal metastases is shown in Fig. 3. Patients with mixed or sclerotic lesions had significantly better survival compared with those with lytic lesions and those with skeletal involvement documented by bone scintigraphy ($p=0.03$ and 0.005 respectively). The median survival after documentation of skeletal metastases were 9 months, 5 months and 5 months respectively.

Discussion

This study confirmed the reported experience (Moench et al, 1972; Hoppe et al, 1976; Merino et al, 1977; Mesic et al, 1981) that for nasopharyngeal carcinoma the skeleton is the most common site of distant involvement.

Table II. Total number of skeletal regions with symptomatic metastases

Number of skeletal regions	Number of patients
1	61 (43.3%)
2	41 (29.1%)
3	19 (13.5%)
4	14 (9.9%)
5	4 (2.8%)
>5	2 (1.4%)

The common sites of metastatic skeletal involvement by nasopharyngeal carcinoma conform to that described by Huang (1980) and the general pattern as described for other metastatic tumours, namely the spine, the pelvis, the ribs and the humerus and femur (Tofe et al, 1975; Krishnamurthy et al, 1977; Murray & Jacobson, 1977; Murray & Watt, 1987). This pattern of relative frequency was maintained in the second region of involvement, as well as the total number of patients with symptomatic lesions in each region. The axial skeleton and the proximal long bones, which contain red marrow, are expected to be preferentially affected as most skeletal metastases are haematogenous in origin, whether by retrograde venous flow or via the general arterial circulation after venous or lymphatic access (Tofe et al, 1975). The access of the nasopharynx to the prevertebral venous plexus (Batson, 1942) does not make the distribution of skeletal metastases different from other tumours with no access to the prevertebral venous plexus, but perhaps accounts for the higher incidence of skeletal metastases compared with other head and neck tumours.

While the majority of bony metastases are osteolytic in general, sclerotic metastases are well known for prostatic and breast cancers. Other primary sites that are well recognized as being associated with sclerotic metastases include lung (Napoli et al, 1973), pancreas (Joffe & Antonioli, 1978), carcinoid (Peavy et al, 1973), urinary bladder (Evison et al, 1981), melanoma (Fon et al, 1981), colon (Seife, 1973) and soft tissue sarcoma (Wong et al, 1982). Although they can be associated with any metastatic cancer, the high frequency of mixed and sclerotic metastases in the present series again makes nasopharyngeal carcinoma unusual among head and neck tumours.

Another interesting finding in the present study is the significantly better prognosis of patients with mixed or sclerotic bony metastases compared with patients with lytic bony metastases. Although it has been a common belief that osteoblastic metastases tend to have a slower growth rate compared with osteolytic metastases, it has not been well substantiated (Greenfield, 1986). In their study of bone metastases from breast cancer, Barry et al (1981) showed that a lytic pattern correlated with progressive tumour growth, whereas blastic pattern correlated with clinical remission. The present study adds to the literature by showing that mixed or sclerotic bony metastases of nasopharyngeal carcinoma presented later compared with lytic lesions and also that patients with mixed or sclerotic metastases had significantly better survival after the diagnosis of skeletal involvement.

Acknowledgments

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References

ARONS, M. S. & SMITH, R. R., 1961. Distant metastasis and local recurrence in head and neck cancer. *Annual of Surgery, 154*, 235–240.

BARRY, W. F. JR, WELLS, S. A. JR, COX, C. E. & HAAGENSEN, D. E. JR, 1981. Clinical and radiographic correlations in breast cancer patients with osseous metastases. *Skeletal Radiology, 6*, 27–32.

BATSON, O. V., 1942. Veins of pharynx. *Archives of Otolaryngology, 36*, 212–219.

BEDWINEK, J. M., PEREZ, C. A. & KEYS, D. J., 1980. Analysis of failures after definitive irradiation of epidermoid carcinoma of the nasopharynx. *Cancer, 45*, 2725–2729.

BERGER, D. S. & FLETCHER, G. H., 1971. Distant metastasis following local control of squamous cell carcinoma of the nasopharynx, tonsillar fossa, and base of the tongue. *Radiology, 100*, 141–143.

CASTIGLIANO, S. G. & ROMINGER, C. J., 1954. Distant metastasis from carcinoma of the oral cavity. *American Journal of Roentgenology, 72*, 997–1006.

EVISON, G., PIZZY, N. & ROYLANCE, J., 1981. Bone formation associated with osseous metastases from bladder carcinoma. *Clinical Radiology, 32*, 303–309.

FON, G. T., WONG, W. S., GOLD, R. H. & KAISER, L. R., 1981. Skeletal metastases of melanoma: radiographic, scintigraphic, and clinical review. *American Journal of Roentgenology, 137*, 103–108.

GREENFIELD, G. B., 1986. Cardinal roentgen features. In *Radiology of Bone Disease*, 4th edn by G. B. Greenfield (J. B. Lippincott, Philadelphia), pp. 393–552.

HOPPE, R. T., GOFFINET, D. R. & BAGSHAW, M. A., 1976. Carcinoma of the nasopharynx, eighteen years' experience with megavoltage radiation therapy. *Cancer, 37*, 2605–2612.

HOYE, R. C., HERROLD, K. M., SMITH, R. R. & THOMAS, L. B., 1962. A clinicopathological study of epidermoid carcinoma of the head and neck. *Cancer, 15*, 741–749.

HUANG, S. C., 1980. Nasopharyngeal cancer: a review of 1605 patients treated radically with cobalt 60. *International Journal of Radiation Oncology, Biology, Physics, 6*, 401–407.

JOFFE, N. & ANTONIOLI, D. A., 1978. Osteoblastic bone metastases secondary to adenocarcinoma of the pancreas. *Clinical Radiology, 29*, 41–46.

KRISHNAMURTHY, G. T., TUBIS, M., HISS, J. & BLAHD, W. H., 1977. Distribution pattern of metastatic bone disease: a need for total body skeletal image. *Journal of the American Medical Association, 237*, 2504–2506.

MERINO, O. R., LINDBERG, R. D. & FLETCHER, G. H., 1977. An analysis of distant metastases from squamous cell carcinoma of the upper respiratory and digestive tracts. *Cancer, 40*, 145–151.

MESIC, J. B., FLETCHER, G. H. & GOEPFERT, H., 1981. Megavoltage irradiation of epithelial tumors of the nasopharynx. *International Journal of Radiation Oncology, Biology, Physics, 7*, 447–453.

MOENCH, H. C. & PHILLIPS, T. L., 1972. Carcinoma of the nasopharynx, review of 146 patients with emphasis on radiation dose and time factor. *American Journal of Surgery, 124*, 515–518.

MURRAY, R. O. & JACOBSON, H. G., 1977. Malignant neoplasms. In *The Radiology of Skeletal Disorder. Exercises in diagnosis, Vol. I*, second edn. Ed. by R. O. Murray and H. G. Jacobson (Churchill Livingstone, London), pp. 581–649.

MURRAY, R. O. & WATT, I., 1987. Tumours and tumour-like conditions of bone. In *Textbook of Radiology and Medical Imaging, Vol. I*, fourth edn. Ed. by D. Sutton (Churchill Livingstone, London), pp. 136–196.

NAPOLI, L. D., HANSEN, H. H., MUGGIA, F. M. & TWIGG, H. L., 1973. The incidence of osseous involvement in lung cancer, with special reference to the development of osteoblastic changes. *Radiology, 108*, 17–21.

O'BRIEN, P. H., CARLSON, R., STEUBNER, E. A. & STALEY, C. T., 1971. Distant metastasis in epidermoid cell carcinoma of the head and neck. *Cancer, 27*, 304–307.

PEAVY, P. W., ROGERS, J. V. JR, CLEMENTS, J. L. JR & BURNS, J. B., 1973. Unusual osteoblastic metastases from carcinoid tumors. *Radiology, 107*, 327–330.

PEREZ, C. A., ACKERMAN, L. V., MILL, W. B., OGURA, J. H. & POWERS, W. E., 1969. Cancer of the nasopharynx, factors influenceing prognosis. *Cancer, 24*, 1–17.

PROBERT, J. C., THOMPSON, R. W. & BAGSHAW, M. A., 1974. Patterns of spread of distant metastasis in head and neck cancer. *Cancer, 33*, 127–133.

RUBENFELD, S., KAPLAN, G. & HOLDER, A. A., 1962. Distant metastasis from head and neck cancer. *American Journal of Roentgenology, 87*, 441–448.

SEIFE, B., 1973. Osseous metastases from carcinoma of the large bowel. *American Journal of Roentgenology, 119*, 414–418.

SHAM, J. S. T., CHOY, D. & CHOI, P. H. K., 1990. Nasopharyngeal carcinoma: the significance of neck node involvement in relation to the pattern of distant failure. *British Journal of Radiology, 63*, 108–113.

SHAM, J. S. T. & CHOY, D., 1990. Prognostic factors of nasopharyngeal carcinoma: a review of 759 patients. *British Journal of Radiology, 63*, 51–58.

THOMPSON, R. W., DOGGET, R. L. S. & BAGSHAW, M. A. A., 1970. Ten-year experience with linear accelerator irradiation of cancer of the nasopharynx. *Radiology, 97*, 149–155.

TOFE, A. J., FRANCIS, M. D. & HARVEY, W. J., 1975. Correlation of neoplasms with incidence and localization of skeletal metastases: an analysis of 1355 diphosphonate bone scans. *Journal of Nuclear Medicine, 16*, 986–989.

WONG, W. S., KAISER, L. R., GOLD, R. H. & FON, G. T., 1982. Radiographic features of osseous metastases of soft tissue sarcoma. *Radiology, 143*, 71–74.

1990, *The British Journal of Radiology*, 63, 206–208

Radiotherapy of Morbus Gorham–Stout: the biological value of low irradiation dose

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Abstract. Morbus Gorham–Stout is a very rare disease. A patient with this disease was treated at the University Clinic of Radiobiology in Vienna. The clinical and radiological findings place special emphasis on the radiotherapeutic treatment, and the biological basis of the recommended dose is discussed.

The first case of progressive bone osteolysis combined with a soft-tissue tumour was reported in the Boston Medical and Surgical Journal (Jackson, 1838), with a follow-up in the same journal (Jackson, 1872). This was the only case observed before X rays were discovered. Another case was reported by Branch (1945), and an overview of patients with vanishing bones was made by Gorham and Stout (1955).

They concluded that the progressive osteolysis is always associated with an angiomatosis of the blood and sometimes angiomas of lymphatic vessels. The use of radiotherapy and the appropriate radiation doses are controversial, as discussed in the literature (Hoffman et al, 1980; Bek et al, 1981; Polivy & Zimbler, 1983). In our view, radiotherapy in Morbus Gorham–Stout is the preferable treatment. Here we attempt to answer the question as to why a relatively low dose of irradiation can be effective in this disease.

Clinical and radiological findings

The disease may imitate a locally aggressive tumour, involving bones and adjacent tissues, although there are no other attributes of neoplastic disease or inflammatory process. The disease is neither inherited nor congenital. Fractures and pain in the bones may be present (Hambach et al, 1958; Sage & Allen, 1974; Heyden et al, 1977; Ross et al, 1978; Listewnik et al, 1986).

In a few of the reported cases, radiographs depict early massive osteolysis. Johnson and McClure (1958) distinguished between an intraosseous and an extraosseous stage: in the early intraosseous stage, massive osteolysis resembles a "non-descript patchy osteoporosis", but later its appearance becomes that of any expanding non-sclerosing intramedullary lesion.

There is no neoplastic osteogenesis or significant reactive bone formation. Having produced a disruption in the cortex of the encasing bone, the angioma invades and proliferates in the surrounding soft tissues. Bony resorption continues, but is now caused by the extraosseous as well as by the intraosseous component of the angioma. Confirmation of the roentgen diagnosis of massive osteolysis can be achieved by arteriography and phlebography.

It has been stated that irradiation can stop the osteolysis, but the disease may be arrested spontaneously too (Johnson & McClure, 1958; Campbell et al, 1975; Heyden et al, 1977; Ross et al, 1978; Feigel et al, 1981; Kolar et al, 1981; Len & Brunner, 1981).

Therapeutic treatment

In most cases, bone resorption stops spontaneously. Many treatment modalities have been reported in cases of progressing disease. The two principal ones are surgical resection and radiotherapy. Other treatments which have been used include vitamin D, parathyroid hormone, androgens, calcium, adrenal extracts, vitamin B_{12} and others. Sympathectomy was used in one patient without any effect on the disease (Leriche, 1937).

Surgical treatment of massive osteolysis has consisted of amputation and local resection, with and without replacement prostheses or bone grafts. Attempts at bone grafting have met with variable success (Aston, 1958; Butler et al, 1958; Halliday et al, 1964). There are also several reports showing involvement of grafts by the osteolytic process (Aston, 1958).

In recent years the use of early radiotherapy has become more popular, in some instances with remarkable success (Murphy, 1978; Henck, 1979; Hoffman et al, 1980; Bek et al, 1981; Polivy & Zimbler, 1983).

Despite the fact that many cases of bone resorption stop spontaneously, radiotherapy should be carried out as soon as possible after diagnosis, giving the destruction no time to spread. In planning a radiotherapy treatment, the volume should include not only the affected bones but also the surrounding soft tissues showing clinical or, better still, angiographic or computed tomographic signs of angiomatous invasion. Normally anteroposterior fields are used. If photons of higher energy (1 MeV) are unavailable or anteroposterior diameter is greater than 22 cm, a multiple field technique should be used. One should avoid the perineum or block parts of the vulva or scrotum if possible.

Recalcification, if it occurs, takes 4 months to become evident (Libschitz & Hortobagyi, 1981).

Biological basis of applied radiation dose

Endothelial cells of proliferating capillaries or capillary-like vessels are extremely radiosensitive (Reinhold & Buisman, 1973; Reinhold, 1974). The classic histological appearance of vessel lesion in irradiated tissue is well documented. It is similar to the abnormalities found as a consequence of hypertension; hypertension and irradiation damage to vessels would appear to be linked in some way. Byrom (1963) reported the presence of irregularly spaced areas of constriction and dilation in the vessels of hypertensive animals. It has been suggested that similar changes could occur in irradiated blood vessels (Hopewell, 1968; Hopewell & Wright, 1970), the constrictions being formed by clones of vessel wall elements, *i.e.* endothelial or muscle cells. These clones of cells originate from the irregularly spaced reproductively viable cells that remain after irradiation. At the time of irradiation the majority of cells in the vessels are rendered reproductively non-viable. Cell loss occurs as these cells attempt to divide, stimulating the viable cells to produce irregularly spaced clones of cells along the length of a blood vessel. If the radiation dose increases, the number of viable cells is reduced until no occlusive reactions are possible (Hopewell, 1974).

The observation of a maximum reduction in blood flow in mouse tail skin after 30 Gy and no modification after higher doses could be explained by the absence of proliferative endothelial cells (de Ruiter & van Pútten, 1975).

Case report

The patient, born in 1964, was admitted to the University Clinic for Radiotherapy in 1980 because of increasing pain in the right hip and seat which had continued for 2 years. A radiograph obtained elsewhere in March 1980 revealed quite discernible osteolytic destruction of the right os ilium with evidence of pathological fracture of the right os ischium.

A bone survey disclosed no other areas of damage. On removal of a bone sample from the tuber ischii, serous fluid exuded from the tissues immediately outside the tuber ischii, giving the impression that a cystic process was present in the abdominal cavity. A contrast medium injection in this area by means of the inserted radon drain showed a massive colouring right into the retroperitoneal cavity. These results helped to establish the presence of a lymphangioma. Specimens of the partially destroyed bone showed an increased content of thin-walled vessels, some containing erythrocytes.

In April 1980 the angiectatic tumour and also some retroperitoneal enlarged lymph nodes were resected at the orthopaedic department. Histologically the lymph nodes showed no evidence of disease. A post-operative lymphangiogram was normal, as was a subsequent aortogram. No obvious connection with the vascular or lymphatic circulation was noted. Post-operatively the patient was free from complications, and used crutches to ease the strain. The patient was kept under observation at the orthopaedic department. Subsequent radiographic check-ups continued to show a relatively rapid progression of osteolytic changes. For this reason, radiotherapy of the affected pelvic bones was started.

In our patient's case, radiotherapy was started at the time of demonstrable clinical and roentgenological progression.

Our patient received 30.6 Gy γ rays via opposing 22/14 cm ports in 17 days (single dose: 180 cGy, target volume–skin distance: 8 cm) ventral and dorsal, with sufficient margin of tissues. At the end of the radiation treatment the pains in the area of the right hip were considerably relieved. The only symptom present was slight pain due to pressure of weight.

Following radiotherapy, our patient's radiograph showed slight recalcification. The arrest of the osteolytic process can therefore be regarded as an effect of radiotherapy.

Discussion

There is a controversy concerning different treatment modalities for Morbus Gorham–Stout, especially in the area of radiotherapy. Poilleux and Codron (1960) report a patient for whom no active therapy was attempted. This ended in the devastation of the pelvic bones with a large number of pathological fractures and the patient's invalidity. Because of the rarity of this disease, the long-term effectiveness of radiation therapy cannot as yet be critically evaluated.

An analysis of the literature reveals different opinions concerning the effect of radiotherapy: authors describing radiotherapy as ineffective used total doses ranging from a few cGy up to 20 Gy. Where a higher total dose was applied: up to 30 Gy or more, the effect was quite remarkable, as with our patient.

Arrest of the osteolytic process and partial recalcification of the destroyed bone could be seen (Knoch, 1963; Heyden et al, 1977). The radiation dose therefore seems to be essential. In most cases the greatest part of the soft-tissue tumour is removed. Moreover, a dose of about 40 Gy is regarded as sufficient for benign tumours.

Biological considerations give a hint as to what total dose should be used in this disease. On increasing the radiation dose, the number of viable cells is reduced until no occlusive reactions are possible. The observation by Casarett (1964) that vascular occlusive changes by endothelial cells are inhibited and parenchymal damage reduced after exposure to high doses in polonium irradiated rat kidneys can be explained on the basis that only a negligible number of viable cells remain to form clones under these conditions.

A similar explanation was used to explain the reduction in vascular damage in rat brains treated with 4000 R as compared with those receiving 3000 R (Hopewell, 1974). This would also explain why hypertension loses its "radiosensitizing" effect, although it has been suggested that endothelial cells are responsible for vessel occlusion and vascular spasm (as is suggested for hypertension).

This is supported by Bosniak et al (1969) who reported vascular spasm in irradiated vessels using an arteriographic technique. Bullough (1971) agrees that radiation therapy would appear to be a rational approach to the treatment of Gorham's disease but one has to bear in mind the inherent dangers of inducing sarcoma.

Megavoltage irradiation, which produces equal absorption of energy in bone and soft tissue, induces fewer bone sarcomas than orthovoltage irradiation, which has a higher absorption in bone compared with soft tissue (Tountas et al, 1979).

The dose used in Morbus Gorham–Stout is the same as in juvenile angiofibroma, and the risk of radiation-induced cancer following treatment of juvenile angiofibroma is very low.

None of 47 angiofibroma patients irradiated at the Radiumhemmet who were followed for between 10 and 40 or more years developed a radiation-induced cancer (Jereb et al, 1970) and there were no instances among 45 irradiated patients at Princess Margaret Hospital with from 2 to 20 years of follow-up (Fitzpatrick, 1970, Fitzpatrick et al, 1980).

In conclusion, Gorham–Stout's syndrome is a rare and clinically serious disease, which, if untreated, can be mutilating despite the fact that spontaneous arrest can occur. Early irradiation of the appropriate selected volume of tissues using adequate doses of radiation can stop osteolysis and can achieve at least partial recalcification of the destroyed bone tissue.

References

Aston, J. N., 1958. A case of massive osteolysis of the femur. *Journal of Bone and Joint Surgery, 40B*, 514.

Bek, V., Haicl, Z., Kolář, J. & Bednář, B., 1981. Radiotherapy in massive angiomatous osteolysis (Gorham–Stout's syndrome), *Strahlentherapie, 157*, 813–818.

Bosniak, N. A., Hardy, N. A., Quint, J. & Ghossein, N. A., 1969. Demonstration of the effects of irradiation on canine bowel using in vivo photographic magnification angiography. *Radiology, 93*, 1361–1368.

Branch, H. E., 1945. Acute spontaneous absorption of bone, report of a case involving a clavicle and scapula. *Journal of Bone and Joint Surgery, 27*, 706.

Bullough, P. G., 1971. Massive osteolysis. *New York State Journal of Medicine, 71*, 2267.

Butler, R. W., McCane, R. A. & Barrett, A. M., 1958. Unexplained destruction of the shaft of the femur in a child. *Journal of Bone and Joint Surgery, 40B*, 487.

Byrom, F. B., 1963. The nature of malignancy in hypertension disease. *Lancet, ii*, 516–520.

Campbell, J., Almond, H. G. A. & Johnson, R., 1975. Massive osteolysis of the humerus with spontaneous recovery. *Journal of Bone and Joint Surgery, 57*, 238–240.

Casarett, G. W., 1964. Pathology of single intravenous doses of polonium. *Radiation Research Supplement, 5*, 246–321.

Feigel, D., Seidel, L. & Marmor, A., 1981. Gorham's disease of the clavicle with bilateral pleural effusion. *Chest, 79*, 242–244.

Fitzpatrick, P. J., 1970. The nasopharyngeal angiofibroma. *Canadian Journal of Surgery*, 13, 228–235.

Fitzpatrick, P. J., Briant, D. R. & Berman, J. M., 1980. The nasopharyngeal angiofibroma. *Archives of Otolaryngology, 106*, 234–236.

Gorham, L. W. & Stout, A. P., 1955. Massive osteolysis (acute spontaneous absorption of bone, phantom bone, disappearing bone). It's relation to hemangiomatosis. *Journal of Bone Surgery, 37a*, 985–1004.

Halliday D. R., Dahlin, D. C., Pugh D. G. & Young, H. H., 1964. Massive osteolysis and angiomatosis. *Radiology, 82*, 637.

Hambach, K., Pujman, J. & Maly, W., 1958. Massive osteolysis due to hemangiomatosis. *Radiology, 71*, 43.

Henck, F., 1979. Diagnosis: massive osteolyse (vanishing bone disease; Gorham disease) of mandible. *Skeletal Radiology, 3*, 241–243.

Heyden, G., Kindblom, L. G. & Nielsen, J. M., 1977. Disappearing bone disease: a clinical and histological study. *Journal of Bone and Joint Surgery, 59A*, 57.

Hoffman, H. J. & Harwood-Nash D. C., 1980. Massive osteolysis in association with multiple cerebrospinal fluid fistulae. *Canadian Journal of Neurological Science, 7*, 39–44.

Hopewell, J. W., 1968. Effects of ionizing radiation and chemical carcinogens on the mammalian central nervous system (PhD Thesis, University of London).

Hopewell, J. W. & Wright, E. A., 1970. The nature of latent cerebral irradiation damage and its modification by hypertension. *British Journal of Radiology, 43*, 161–167.

Hopewell, J. W., 1974. The late vascular effects of radiation. *British Journal of Radiology, 47*, 157–158.

Jackson, J. B. S., 1838. A singular case of absorption of bone (a boneless arm). *Boston Medical and Surgical Journal, 18*, 368–369.

Jackson, J. B. S., 1872. Absorption of the humerus after fracture. Reported to the Boston Society for Medical Improvement by the various gentlemen under whose observation they had fallen. *Boston Medical and Surgical Journal, 87*, 245–247.

Jereb, B., Änggård, A. & Båryd, I., 1970. Juvenile nasopharyngeal angiofibroma: a clinical study of 69 cases. *Acta Radiologica (Therapy), 9*, 302–310.

Johnson, M. & McClure, J. G., 1958. Observations on Massive Osteolysis, *Radiology, 71*, 28.

Knoch, H. G., 1963. Die Gorham'sche Krankheit aus klinischer Sicht. *Zbl. Chir. 18*, 674.

Leriche, R., 1937. A propos des ostéolyses d'origine indéterminée. *Mém. Acad. de Chir., 63*, 418–421.

Libshitz, H. I. & Hartobagyi, G. N., 1981. Radiographic evaluation of therapeutic response in bone metastases of breast cancer. *Skeletal Radiology, 7*, 159.

Listewnik, M. J., Marzecki, Z. & Kardowski, J., 1986. Disappearing bone disease: massive osteolysis of the ribs treated with radiotherapy. Report of a case. *Strahlentherapie, 162*, 338–341.

Len, H. J. & Brunner, V., 1981. Osteolisierte haemangiomatose nach trauma. *Deutsche Medizinische Wochenscrift, 106*, 1424.

Murphy, J. B., Dohn, H. C. & Carter, B. L., 1978. Massive osteolysis; phantom bone disease. *Journal of Oral Surgery, 36*, 318–322.

Poilleux, F. & Codron, 1960. L'ostéolyse régionale. *Annales de Chirurgie, 14*, 9.

Polivy, K. D. & Zimbler, S., 1983. Massive osteolysis in disappearing bone disease. *Orthopedics, 6*, 1012–1015.

Reinhold, H. S., 1974. Structural changes in blood vessels. *Current Topics in Radiation Research, 10*, 58–74.

Reinhold, H. S. & Buisman, G. H., 1973. Radiosensitivity of capillary endothelium.. *British Journal of Radiology, 46*, 54.

Ross, J. L., Schinella, R. & Shenkman, L., 1978. Massive osteolysis. An unusual cause bone destruction. *American Journal of Medicine, 65*, 367.

de Ruiter, J. & van Pútten, L. M., 1975. Measurement of blood flow in the mouse tail after irradiation. *Radiation Research, 61*, 427–438.

Sage, M. R. & Allen, P. W., 1974. Massive osteolysis. Report of a case. *Journal of Bone and Joint Surgery 65B*, 130.

Tountas, A. A., Fornasier, V. L., Harwood, A. R. & Leung, P. M. K., 1979. Postirradiation sarcoma of bone: A perspective. *Cancer, 43*, 182–187.

1990, *The British Journal of Radiology*, *63*, 209–213

Gastrointestinal histamine and histamine formation capacity after gastric irradiation in mice

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Abstract. Mice were exposed to a single dose of 9 or 15 Gy of X rays directed to the stomach. Histamine and histamine formation capacity (HFC) in the oxyntic region of the stomach were assayed at regular intervals for 7 weeks. After 9 Gy, mean gastric mural histamine fell to 61% of the control value ($p<0.01$) 7 days after irradiation while HFC rose to 172% ($p<0.05$). Both histamine and HFC returned to control values within 2 weeks after irradiation. With 15 Gy, on Day 7, histamine fell to 46% ($p<0.01$) and HFC rose to 260% ($p<0.05$). Histamine concentration remained low (less than half of the control value) while HFC returned to normal. These dose-dependent changes in histamine were observed neither elsewhere in the gut nor in the circulating blood. Further groups of mice were exposed to 3, 6, 9 or 15 Gy to the stomach, with gastric histamine and HFC assayed on Day 7. Histamine concentration was inversely related to dose ($r=-0.59$, $p<0.001$) and HFC was directly dose dependent ($r=0.52$, $p<0.001$). These results suggest that irradiation of the stomach may reduce gastric histamine without inducing a general histamine release. The depletion of the gastric histamine store may explain the inhibitory effect of irradiation of the stomach on gastric acid secretion.

Irradiation of the stomach may result in a prolonged inhibition of acid secretion in both patients and experimental animals (Palmer, 1974; Ragins, 1974). Before the advent of specific histamine H_2-receptor antagonists, gastric irradiation was occasionally used for treatment of peptic ulcer (Palmer, 1974).

The inhibitory mechanism is not clear. Irradiation may impair the local regulatory system for acid secretion. Histamine, a potent secretagogue, is well known to act as a physiological mediator for acid production (Black & Shankley, 1987). In rodents, gastric acid secretion is closely associated with mobilization of gastric mucosal histamine (Kahlson et al, 1973; Lundell, 1975). Secretion of acid is accompanied by a transient depletion of gastric mucosal histamine coupled with an increase in the activity of the enzyme, histidine decarboxylase, which synthesizes histamine to replenish the histamine store (Kahlson et al, 1973). In mice, 7 days after 9 Gy of X rays to the stomach, both the basal and pentagastrin-stimulated acid and histamine secretion were reduced. After the gastric secretion test, the concentration of histamine in the acid-producing region of the stomach was significantly lower than the control value (Man et al, 1988).

The aim of the present study was to investigate the effect of gastric irradiation on the endogenous histamine concentration and histidine decarboxylase activity (an *in vitro* assay of the histamine formation capacity (HFC)) in the acid-producing region of the stomach. A preliminary report has been published (Man et al, 1986).

Materials and methods

Radiation procedures

Female CFLP mice aged 12–20 weeks were anaesthetized with pentobarbitone (0.06 mg/g i.p.). A downward beam of X rays (250 kV, half-value layer (HVL) 1.35 mm Cu and dose rate 1.73 Gy/min, target distance 39 cm) was used to deliver a single dose ranging from 3 to 15 Gy to the stomach (field size 16 × 20 mm), with the rest of the body shielded by 7 mm of lead. To demonstrate that radiation was localized to the stomach, several mice were fed contrast medium, anaesthetized and placed in a Perspex mock-irradiation jig. The lid of the jig had the field of irradiation delineated with fine wire. Radiographs confirmed that the irradiation was confined to and covered the entire stomach.

Time course study

A total of 205 mice were divided into three groups. Group 1 consisted of 29 mice which were unirradiated controls and anaesthetized only. Group 2, 88 mice, received 9 Gy and Group 3, 88 mice, received 15 Gy. Between one and four mice from Group 1, eight from Group 2 and eight from Group 3 were studied twice a week for 2 weeks and then two mice from Group 1, four from Group 2 and four from Group 3 weekly for a further 5 weeks after irradiation. The body weights of the irradiated mice were monitored daily up to Day 20 post-irradiation and compared with those of control mice recorded on the same day.

After overnight fasting, mice were given a lethal dose of pentobarbitone. Blood from the heart was aspirated into a hypodermic syringe and ice-cold saline was then instilled into the lumen of the gastrointestinal tract via the forestomach and the anus. Tissue specimens for histamine assay were taken from along the alimentary

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Table I. Histamine concentrations in oesophagus, proximal and distal duodenum after gastric irradiation ($n=4$)

Day post-irradiation	Oesophagus (nmol/g)		Proximal duodenum (nmol/g)		Distal duodenum (nmol/g)	
	9 Gy Mean ± s.d.	15 Gy Mean ± s.d.	9 Gy Mean ± s.d.	15 Gy Mean ± s.d.	9 Gy Mean ± s.d.	15 Gy Mean ± s.d.
1	35.7 ± 1.5	12.9 ± 7.7	7.4 ± 1.0	6.9 ± 6.3	2.4 ± 0.3	2.2 ± 0.6
4	21.4 ± 8.9	25.8 ± 0.9	10.7 ± 5.3	8.3 ± 4.9	7.0 ± 4.1	6.6 ± 2.8
7	21.1 ± 5.7	21.1 ± 4.0	4.3 ± 2.0	4.9 ± 1.1	3.3 ± 1.0	3.2 ± 0.5
11	14.5 ± 2.9	8.7 ± 4.3	10.3 ± 1.9	13.2 ± 5.8	3.2 ± 1.1	3.8 ± 2.5
14	13.5 ± 3.4	13.0 ± 3.5	7.9 ± 4.0	3.3 ± 1.6	6.3 ± 3.9	1.9 ± 0.4
18	8.6 ± 3.5	21.1 ± 8.5	3.6 ± 1.3	7.8 ± 8.6	3.8 ± 1.9	3.2 ± 1.1
21	8.8 ± 6.4	4.4 ± 1.7	13.4 ± 7.0	7.5 ± 4.7	6.2 ± 4.4	10.0 ± 7.1
28	4.0 ± 5.4	4.4 ± 2.6	9.2 ± 3.6	5.6 ± 2.3	6.0 ± 1.8	3.1 ± 3.3
35	3.0 ± 1.7	2.9 ± 0.7	6.7 ± 2.1	8.7 ± 5.0	2.3 ± 2.1	1.3 ± 0.94
42	6.4 ± 2.4	4.3 ± 3.9	6.1 ± 2.4	4.7 ± 1.5	5.1 ± 7.5	2.5 ± 0.7
49	4.0 ± 1.9	6.6 ± 2.9	8.2 ± 4.7	3.9 ± 0.9	6.7 ± 7.0	— —
Controls ($n=17$)	10.9 ± 10.8		6.8 ± 3.0		6.4 ± 5.5	

tract at well-defined sites following a fixed sequence as follows: (1) colon, immediately above the rectum; (2) ileum, proximal to the ileo-caecal junction; (3) stomach, zymogenic (oxyntic) region as defined by Lee et al (1982); (4) proximal duodenum, between the gastroduodenal junction and the duodenal papilla; (5) distal duodenum, distal to the duodenal papilla and (6) oesophagus, between the oesophago-gastric junction and the level of tracheal bifurcation.

All tissue samples were whole wall specimens, in triplicate, each weighing 20–40 mg (oesophagus, 5–10 mg) and were stored at −20°C until analysis. The entire sampling procedure was completed within 15 min of pentobarbitone injection.

A further 48 mice were divided into two groups. Eight were unirradiated controls, while the rest were given 15 Gy gastric irradiation. On Day 6, 16 test mice, Day 9, 16 mice and Day 12, eight mice, together with two controls each were anaesthetized and killed as above. The stomach was removed "en bloc". A strip from the oxyntic region was sampled as before and stored frozen until analysis.

Dose–response study

Forty mice were divided into five groups given 0, 3, 6, 9 or 15 Gy of X rays respectively. On Day 7, after overnight fasting, the mice were anaesthetized and killed and a strip from the oxyntic region was sampled as above.

Histamine assays

Tissue histamine assay was based on the fluorometric method of Rhode et al (1980) and has been described in detail elsewhere (Man et al, 1984). Gastric specimens were also assayed for histidine decarboxylase activity, *i.e.* the HFC, by a combination of two methods (Taylor

Table II. Histamine concentrations in ileum, colon and blood plasma after gastric irradiation ($n=4$)

Day post-irradiation	Ileum (nmol/g)		Colon (nmol/g)		Plasma (nmol/ml)	
	9 Gy Mean ± s.d.	15 Gy Mean ± s.d.	9 Gy Mean ± s.d.	15 Gy Mean ± s.d.	9 Gy Mean ± s.d.	15 Gy Mean ± s.d.
1	6.9 ± 3.6	4.1 ± 1.4	4.0 ± 0.8	1.6 ± 0.5	0.16 ± 0.05	0.20 ± 0.08
4	2.3 ± 1.3	1.9 ± 0.4	5.0 ± 0.7	1.9 ± 0.4	0.17 ± 0.06	0.18 ± 0.08
7	2.6 ± 0.8	3.0 ± 2.0	3.8 ± 1.0	3.6 ± 1.0	0.18 ± 0.04	0.24 ± 0.09
11	7.7 ± 3.6	3.8 ± 2.6	5.0 ± 1.6	2.8 ± 0.4	0.36 ± 0.12	0.20 ± 0.07
14	5.8 ± 1.5	7.3 ± 2.0	4.0 ± 1.7	3.3 ± 0.8	0.37 ± 0.14	0.10 ± 0.05
18	7.4 ± 0.7	6.8 ± 1.5	3.5 ± 1.2	2.5 ± 1.3	0.28 ± 0.09	0.20 ± 0.00
21	10.8 ± 7.5	13.4 ± 5.1	3.6 ± 2.4	2.7 ± 1.8	0.10 ± 0.02	0.16 ± 0.05
28	13.8 ± 6.9	9.4 ± 8.6	2.9 ± 1.3	1.0 ± 0.1	0.10 ± 0.03	0.15 ± 0.08
35	4.6 ± 4.7	1.9 ± 0.7	1.3 ± 0.2	1.0 ± 0.4	0.11 ± 0.02	0.12 ± 0.05
42	10.2 ± 5.6	8.5 ± 7.2	1.9 ± 0.5	1.0 ± 0.1	0.13 ± 0.04	0.11 ± 0.01
49	4.8 ± 2.5	4.1 ± 1.8	2.9 ± 2.9	1.0 ± 0.5	0.11 ± 0.01	0.13 ± 0.02
Controls ($n=17$)	5.3 ± 6.4		2.7 ± 2.0		0.14 ± 0.05	

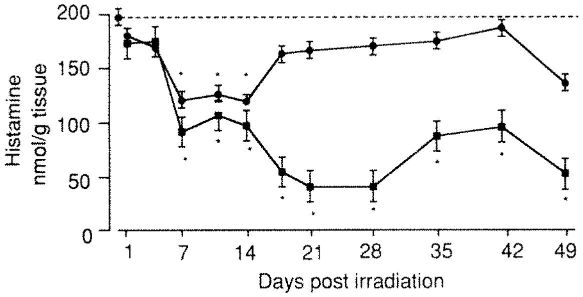

Figure 1. Changes in gastric histamine concentration after irradiation. For unirradiated controls (– – –), $n = 29$; for mice receiving 9 Gy of X rays (●) and 15 Gy (■), from Day 1 to Day 14, $n = 8$ for both test groups and from Day 18, $n = 4$. *Significantly different from control values ($p < 0.05$). Mean ± standard error of mean (SEM).

& Snyder, 1972; Shaff & Beaven, 1979) with minor modification (Man et al, 1984). Histamine in plasma was assayed by an isotopic enzymatic method (Man et al, 1981).

Statistical analysis

Statistical comparisons were made using Student's *t*-test. Correlations were calculated using linear regression analysis. Values for *p* of less than 0.05 were regarded as significant.

Results

No significant changes in body weight were found in mice exposed to 9 Gy X rays. The body weight fell between Day 4 and Day 8 in mice exposed to 15 Gy, reaching a nadir of 95% of control value on Day 6.

Histamine concentrations in the oesophagus, proximal duodenum, distal duodenum, ileum, colon and blood plasma are listed in Tables I and II. No significant differences were observed between the irradiated groups and the unirradiated controls.

Figure 1 illustrates the changes in gastric histamine concentration with time after irradiation. For mice that received 9 Gy of X rays, histamine concentration fell to its lowest point at Day 7. The mean histamine value dropped to 120 nmol per g tissue weight, significantly lower than the mean control value of 195 nmol per g ($p < 0.01$). By Day 18, gastric histamine levels returned to the range of control values. For mice exposed to 15 Gy of X rays, gastric histamine fell by Day 7 to 91 nmol per g, which was significantly lower than the mean control values ($p < 0.01$) and of the mice treated with 9 Gy ($p < 0.05$). Histamine concentration decreased further during the third week after exposure and remained below 50% of control values throughout the rest of the observation period.

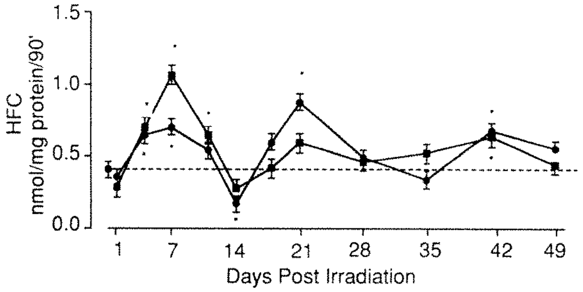

Figure 2. Changes in gastric HFC after irradiation. For unirradiated controls (– – –), $n = 29$; for mice receiving 9 Gy of X rays (●) and 15 Gy (■), from Day 1 to Day 14, $n = 8$ for both test groups and from Day 18, $n = 4$. *Significantly different from control values ($p < 0.05$). Mean ± SEM.

Figure 2 illustrates the changes in gastric HFC at various times after irradiation; HFC was elevated in a dose-related fashion during Days 4–11, with a peak on Day 7. In the low dose group, HFC rose to a mean of 0.70 nmol histamine formed per mg protein after 90 min incubation ($p < 0.05$) and in the high dose group to 1.06 nmol per mg protein ($p < 0.05$) compared with the mean control values of 0.41 nmol per mg protein. By Day 18, HFC returned to control values in both groups of irradiated mice. Higher than control values were measured on Days 21 and 42 after 9 Gy and on Day 42 after 15 Gy.

The effect of 15 Gy X rays on gastric histamine and HFC was further studied from Day 6 to Day 12 after irradiation (Table III). Gastric histamine was lower than control value at all times, and significantly so on Day 6 ($p < 0.05$). On Day 6 and Day 9, gastric HFC was significantly higher than the mean control value ($p < 0.05$). In this series of experiments the control mice had lower mean values for gastric histamine and HFC than the former controls, but the differences were not significant.

Figure 3 illustrates the radiation dose responses for gastric histamine concentration (inverse) and gastric HFC (direct). Histamine concentration and HFC were inversely proportional ($r = -0.35$, $p < 0.03$; $y = -65.1x + 225.4$; $\hat{s}_e = 75.2$).

Discussion

Irradiation of the stomach often leads to a prolonged reduction of gastric acid secretion (Palmer, 1974). The inhibitory effect may be a result of radiation damage of the parietal cells. In mice, exposure to single doses of 12–20 Gy of γ rays resulted in destruction of a proportion of the glands (Chen & Whithers, 1972). However, the repair capacity was great, and regeneration began immediately after the initial injury, with the surviving clonogenic cell number doubling every 43 h.

An alternative view is that radiation may damage the regulatory system for acid secretion. Histamine has long been recognized as a local mediator of gastric secretion (Code, 1965). High concentration of histamine can be found in the acid-producing part of the stomach in all animal species (Lorenz et al, 1973). Specific histamine H_2-receptor antagonists can block acid secretion efficiently (Lundell, 1975). Acid output is associated with gastric histamine release (Kahlson et al, 1973; Lundell, 1975; Man et al, 1981). Kinetic studies of specific H_2-receptor agonists and antagonists, using an isolated

Table III. Effect of 15 Gy gastric irradiation on gastric histamine and HFC

Day post-irradiation	*n*	Histamine (nmol/g) Mean ± s.d.	HFC (nmol/mg prot/90′) Mean ± s.d
6	16	116.4 ± 28.8^a	0.48 ± 0.13^a
9	16	127.3 ± 50.2	0.47 ± 0.23^a
12	8	130.2 ± 37.7	0.40 ± 0.14
Controls	8	169.3 ± 54.2	0.28 ± 0.11

^{a}Significantly different from control values, $p < 0.05$.

mouse stomach model, support the hypothesis that histamine may be the principal mediator in gastric acid secretion (Black & Shankley, 1987).

The present study confirmed that in mice, the acid-producing part of the stomach has the highest histamine concentration in the alimentary canal (Tables I, II and III). Gastric irradiation induced a dose-related depletion of the local histamine store but did not affect the other parts of the alimentarty tract in a similar dose-dependent fashion. The statistically insignificant tendency for an increase in oesophageal histamine during the first 2 weeks after exposure (Table I) may be a result of the inclusion of distal oesophagus in the irradiated volume. However, higher doses than those used in the present experiments are required to induce ulcerative oesophagitis which takes approximately a week to develop and lasts a few days only (Michalowski & Hornsey, 1986).

In the present study, 9 Gy of X rays resulted in a fall in gastric histamine concentration during 4–11 days post-irradiation with the lowest value on Day 7, and recovery to levels lower than but not significantly different from control values by Day 18. In a previous *in vivo* study, on Day 7 after the same dose of X rays to the stomach, basal and pentagastrin stimulated acid output were significantly reduced (Man et al, 1988). Preliminary data showed that on Day 42 basal and stimulated acid output were lower than but not significantly different from control values (Gompertz et al, 1988). Thus the changes in gastric histamine concentration paralleled those of acid secretion.

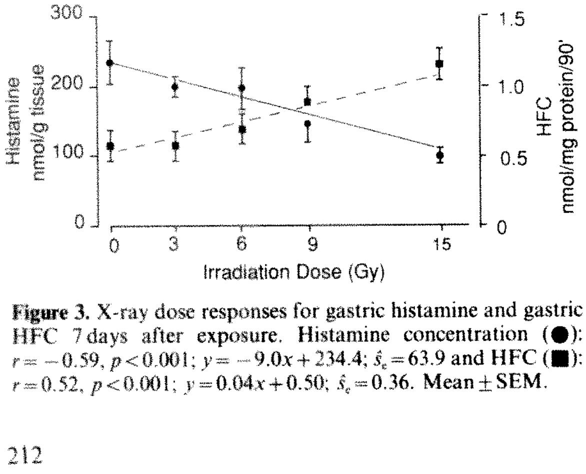

Figure 3. X-ray dose responses for gastric histamine and gastric HFC 7 days after exposure. Histamine concentration (●): $r = -0.59$, $p < 0.001$; $y = -9.0x + 234.4$; $\hat{s}_e = 63.9$ and HFC (■): $r = 0.52$, $p < 0.001$; $y = 0.04x + 0.50$; $\hat{s}_e = 0.36$. Mean ± SEM.

In the present study, in mice that received 15 Gy, gastric histamine concentration dropped to a trough on Day 7 (Day 6 in the second series of time course study). The fall was associated with a transient loss of body weight between Day 4 and Day 8. However, histamine failed to recover and remained at levels less than 50% of those observed in controls. This prolonged reduction of gastric histamine may lead to inhibition of acid secretion even greater than in the low dose group, histamine and acid output being directly related.

Gastric irradiation also induced a rise in the rate of histamine synthesis, as estimated by the *in vitro* assay of HFC. During the first week post-irradiation HFC rose but returned to control values in the second week. On Day 7, HFC was directly correlated with the dose of X rays but was inversely related to the concentration of gastric histamine. This suggests that as gastric histamine falls the enzyme responsible for histamine synthesis is activated as the stomach attempts to replenish its histamine store. For mice that received 9 Gy X rays, both gastric histamine and HFC returned to control values 2 weeks after irradiation. With 15 Gy X rays, gastric histamine remained low while HFC values were generally not different from controls. This suggests that the gastric histamine storage, but not histamine formation, may be permanently damaged by the high dose of irradiation. In all the groups studied, including control groups, the assayed HFC values were consistently more variable than histamine concentration.

In rats the histidine decarboxylase activity in the glandular stomach 1 day after a dose of 20 Gy whole-body X-irradiation was not different from non-irradiated controls that had been fasted for 24 h (Kobayshi & Maudsley, 1972). Similarly, in the present study, 1 day after X-irradiation to the stomach, gastric histidine decarboxylase activity was not significantly different from the non-irradiated, fasted mice. However, X-irradiation limited to the stomach induced a dose-related rise in the activity of the enzyme in the oxyntic region of mouse stomach 7 days after irradiation. It is not known whether whole-body irradiation produces a similar effect of delayed potentiation on the activity of the enzyme which is responsible for histamine synthesis.

In mice, gastric histamine is stored in histamine-immunoreactive endocrine cells and mast cells (Håkanson et al, 1986). The endocrine cells, identified as enterochromaffin-like (ECL) cells, are found almost exclusively in the acid-producing part of the stomach and localized in the basal third of the oxyntic glands whereas mast cells are mainly found in the submucosa (Håkanson et al, 1986). The histamine-forming enzyme, histidine decarboxylase, is also confined to the ECL cells (Aures et al, 1970). Thus histamine is not only stored but also produced at the same site. Radiation damage to the histamine-storing cell may lead to histamine release and to activate histamine synthesis simultaneously. Detailed histochemical studies are necessary to elucidate the effect of irradiation on the gastric histamine-storing cells.

In conclusion, irradiation of the stomach induced local mobilization of gastric histamine. The extent of depletion of the histamine stores and the inability to recover to the normal concentration after 15 Gy of X rays may explain the observed long-term inhibitory effect of irradiation on gastric acid secretion.

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References

AURES, D., HÅKANSON, R. & OWMAN, Ch., 1970. Formation and storage of amines in endocrine cells of gastric mucosa. *Journal of Neuro-Visceral Relations, 31*, 337–349.

BLACK, J. W. & SHANKLEY, N. P., 1987. How does gastrin act to stimulate oxyntic cell secretion? *Trends in Pharmacological Sciences, 8*, 486–490.

CHEN, K. Y. & WITHERS, H. R., 1972. Survival characteristics of stem cells of gastric mucosa in C_3H mice subjected to localized gamma irradiation. *International Journal of Radiation Biology, 21*, 521–534.

CODE, C. F., 1965. Histamine and gastric secretion; a later look, 1955–1965. *Federation Proceedings, 24*, 1311–1321.

GOMPERTZ, R. H. K., MAN, W. K., LI, S. K., BATTEN, J., SPENCER, J., BARON, J. H. & MICHALOWSKI, A. S., 1988. Irradiation of the mouse stomach leads to long lasting, selective inhibition of acid secretion by an indirect mechanism. *International Journal of Radiation Biology, 54*, 854.

HÅKANSON, R., BOTTCHER, G., EKBLAD, E., PANULA, P., SIMONSSON, M., DOHLSTEN, M., HALLBERG, T. & SUNDLER, F., 1986. Histamine in endocrine cells in the stomach. *Histochemistry, 86*, 5–17.

KAHLSON, G., ROSENGREN, E. & SVENSSON, S. E., 1973. Histamine and gastric secretion with special reference to rat. In *The Pharmacology of Gastrointestinal Motility and Secretion, Vol. 1*, ed. by P. Holton (Pergamon Press, Oxford) pp. 41–102.

KOBAYASHI, Y. & MAUDSLEY, D. V., 1972. The response of histidine decarboxylase activity of rat stomach to X-irradiation. *Radiation Research, 50*, 301–308.

LEE, E. R., TRASLER, J., DWIVEDI, S. & LEBLOND, C. P., 1982. Division of the mouse gastric mucosa into zymogenic and mucous regions on the basis of gland features. *American Journal of Anatomy, 164*, 187–207.

LORENZ, W., MATEJKA, E., SCHMAL, A., SEIDEL, W., REIMANN, H. J., UHLIG, R. & MANN, G., 1973. A phylogenetic study on the occurrence and distribution of histamine in the gastrointestinal tract and other tissues of man and various mammals. *Comparative & General Pharmacology, 4*, 229–250.

LUNDELL, L., 1975. Elucidation by a H_2-receptor antagonist of the significance of mucosal histamine mobilization in exciting acid secretion. *Journal of Physiology, 244*, 365–383.

MAN, W. K., SAUNDERS, J. H., INGOLDBY, C. & SPENCER, J., 1981. Effect of pentagastrin on histamine output from the stomach in patients with duodenal ulcer. *Gut, 22*, 916–922.

MAN, W. K., BOESBY, S. & SPENCER, J., 1984. Gastric mucosal histamine, histamine formation capacity (HFC) and plasma gastrin after cysteamine administration. *British Journal of Experimental Pathology, 65*, 759–765.

MAN, W. K., MICHALOWSKI, A., LI, S. K., BARR, J. & BURGIN, J., 1986. Gastrointestinal histamine after gastric irradiation in the mouse. *Agents and Actions, 18*, 210–213.

MAN, W. K., GOMPERTZ, R. H. K., LI, S. K., MICHALOWSKI, A., BARON, J. H. & SPENCER, J., 1988. Effect of gastric irradiation on gastric secretion and histamine in mice. *Agents and Actions, 23*, 297–299.

MICHALOWSKI, A. & HORNSEY, S., 1986. Assays of damage to the alimentary canal. *British Journal of Cancer, 53, Suppl. VII*, 1–6.

PALMER, W. L., 1974. Gastric irradiation in peptic ulcer. In *Gastric Irradiation in Peptic Ulcer*, ed. by W. L. Palmer (The University of Chicago Press, Chicago), pp. 139–150.

RAGINS, H., 1974. External irradiation: experimental aspects. In *Gastric Irradiation in Peptic Ulcer*, ed. by W. L. Palmer (The University of Chicago Press, Chicago), pp. 13–30.

RHODE, H., LORENZ, W., TROIDL, H., REIMANN, H. J., HAFNER, G. & WEBER, D., 1980. Histamine and peptic ulcer: influence of sample-taking on the precision and accuracy of fluorometric histamine assay in the biopsies of human gastric mucosa. *Agents and Actions, 10*, 175–185.

SHAFF, R. E. & BEAVEN, M. A., 1979. Increased sensitivity of the enzymatic isotopic assay of histamine: measurement of histamine in plasma and serum. *Analytical Biochemistry, 94*, 425–430.

TAYLOR, K. M. & SNYDER, S. H., 1972. Isotopic microassay of histamine, histidine, histidine decarboxylase and histamine methyltransferase in brain tissue. *Journal of Neurochemistry, 19*, 1343–1358.

1990, *The British Journal of Radiology*, 63, 214–218

An analysis of personnel dose records which justifies the application of cost-benefit analysis techniques in the design of an afterloading facility and the use of controlled areas and systems of work within suite to control occupational exposure

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Abstract. The sealed source operational policies employed at the Bristol Radiotherapy and Oncology Centre were originally designed to meet the requirements of the 1972 Code of Practice by ensuring that individual personnel doses were kept below the relevant quarterly and annual dose limits. In 1982–1983, measures were taken to improve personnel radiation safety within the brachytherapy treatment facility by (a) making preparations for the introduction of Selectron medium-dose-rate (MDR) afterloading systems at the centre for intracavitary brachytherapy and (b) reviewing the operational policies to ensure that they meet the more stringent requirements of the ALARA (as low as reasonably achievable) principle, a principle subsequently embodied in the 1985 UK Ionising Radiations Regulations (IRR 85). When considering the implications of making existing single-bedded side wards, originally designed for low-dose-rate brachytherapy and suitable for the new systems, the cost of the extra protection required to reduce the instantaneous dose rate in the ward corridors adjacent to the treatment room to less than 7.5 μSv h^{-1} had to be determined. On the basis of the cost-benefit analysis, it was decided not to provide additional shielding but rather to introduce administrative controls based on local rules which contained systems of work and the operational policies for the afterloading systems. After using the MDR afterloading systems for 2 years, a period in which there has also been a marked increase in interstitial brachytherapy, an analysis was made of the doses received by nursing staff over the past 8 years. This has shown that, in spite of higher dose rates in the corridor areas because of the use of an MDR system and the increase in interstitial techniques, the doses to ward nurses have been significantly reduced by encouraging staff to comply with the ALARA principle and the introduction of afterloading systems.

Conventional manual intracavitary brachytherapy techniques involve patients who are undergoing treatment with typically 100–125 milligrams of radium or radium equivalent (mg Ra eq) while, for interstitial techniques, activities of 15–40 mg Ra eq are used. In such cases nursing staff are required to work in areas where the instantaneous dose rate (IDR) at 1 m can be as high as 1 mSv h^{-1}. In order to observe the ALARA (as low as reasonably achievable) principle, a system of work restricting the time that can be spent by any member of staff in these regions of high dose rate must be used, so that individual and collective doses are not excessively high. As a means of reducing doses to personnel, existing operational sealed source policies were reviewed in 1983 to ensure that they were in line with the ALARA principle.

Protection considerations for room design and systems of work

When authorization was given in 1982 to purchase two medium-dose-rate (MDR) Selectron systems, a study was made of the protection requirements to treat patients in the designated rooms with a regime where the source activities to be used are typically 200–250 mg Ra eq. This naturally has the effect of increasing the IDR at 1 m from the patient to 2 mSv h^{-1}. Whilst MDR techniques increase the dose rate, it should be noted that the overall cumulative dose at any given point during the course of treatment is approximately 10–20% lower, since the prescribed dose to the patient has to be reduced by this amount to achieve the same biological effect (Hunter, 1985).

The brachytherapy treatment facility designed for the Bristol Radiotherapy and Oncology Centre consisted of eight single-bedded side wards on the second and third floors of the hospital. These wards were originally constructed with 60 cm (2 ft) concrete walls adjacent to the corridor and, where appropriate, between adjoining wards (Fig. 1), but without protection being provided for the outer walls, since these are well above ground level. At the time when the rooms were originally designed, use could be made of occupancy factor in protection calculations, so no protection was incorporated into the doors. Having made the decision to accommodate the two afterloading systems in two rooms on each floor, plans were made to modify the rooms accordingly. Preliminary calculations indicated that, in order to reduce the dose rate in the corridor and the entrances to the wards to the limit set for a "supervised area", *i.e.* to 2.5 μSv h^{-1}, the thickness of the walls

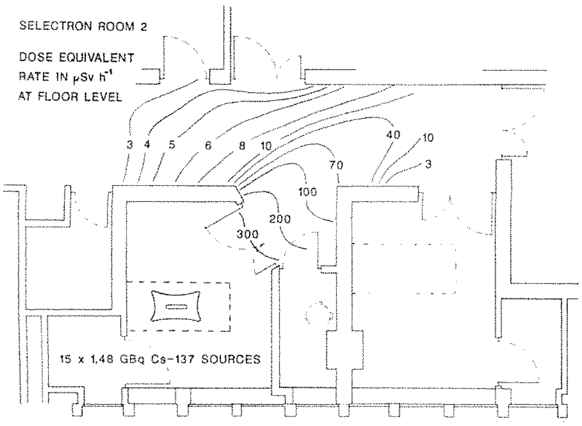

SELECTRON ROOM 2
DOSE EQUIVALENT RATE IN μSv h⁻¹ AT FLOOR LEVEL
3
4
5
6
8
10
40
10
70
3
100
200
300
15 x 1.48 GBq Cs-137 SOURCES

Figure 1. Isodose equivalent curves in Selectron corridor: Ward 61.

would need to be 60 cm of concrete and the doors would need 4 cm of lead. Whilst the existing walls would give adequate protection to meet these requirements, the amount of lead required to provide adequate door protection was totally impracticable. Since under Regulation 6 (IRR 85) engineering control and design features must be used as far as reasonably practicable to reduce the dose rate, the possibility of constructing maze entrances for each single-bedded ward was considered. These mazes would need to provide a barrier equivalent to 60 cm of concrete to reduce the IDR at the room entrance to less than 2.5 μSv h^{-1}, or 30 cm of concrete to reduce the IDR to less than 7.5 μSv h^{-1}, thereby obviating the need to create "controlled areas" other than the treatment rooms themselves. The notional costs of building four entrance mazes was put at £50 000.

Building cost-benefit analysis

To establish the necessity for carrying out such building work, the NPRB approach to evaluating radiation-induced health detriment was followed. In NRPB Report ASP4 (1982), the relevant publication at the time of designing the rooms relating to cost-benefit analysis in radiation protection, the NRPB recommended that the proposed costs of unit collective dose for occupationally exposed staff receiving less than 10% of the annual dose limit for radiation workers should be £4 000 per man Sv, based on 1980 UK prices. Since in this particular case the annual average dose for nursing staff working on the ward in the years 1980–1982 was between 3.0 and 4.0 mSv and the annual collective dose between 0.13 and 0.17 man Sv, depending on the amount of sealed source work being done, then the cost of unit collective dose in this instance was taken to be £4 000 per man Sv.

Using the notional cost of £50 000 to construct the mazes, and making the assumption that this should be amortized over a 15 year period, then the yearly cost over this period at 7% annual discount rate can be obtained by applying an annuity factor, which for this situation has a value of 0.11 (Clark et al, 1981; Fleishman et al, 1983). This factor yields a yearly cost of £5 500. To make the comparison with the cost of unit collective dose, the reduction in dose to the staff by building the mazes must be estimated. It was calculated that a maze would reduce the dose rate at the entrance down to 3% of the original amount. Patients undergoing brachytherapy require nursing care, but nursing staff spend only a small proportion of their time in the area of high dose rate at the entrance to the room: less than 1 nurse-hour per day. It was therefore estimated that the dose reduction due to a maze would be only 5% of the yearly collective dose, which for 1982 was 0.132 man Sv. Thus the dose reduction due to the building of a maze would be

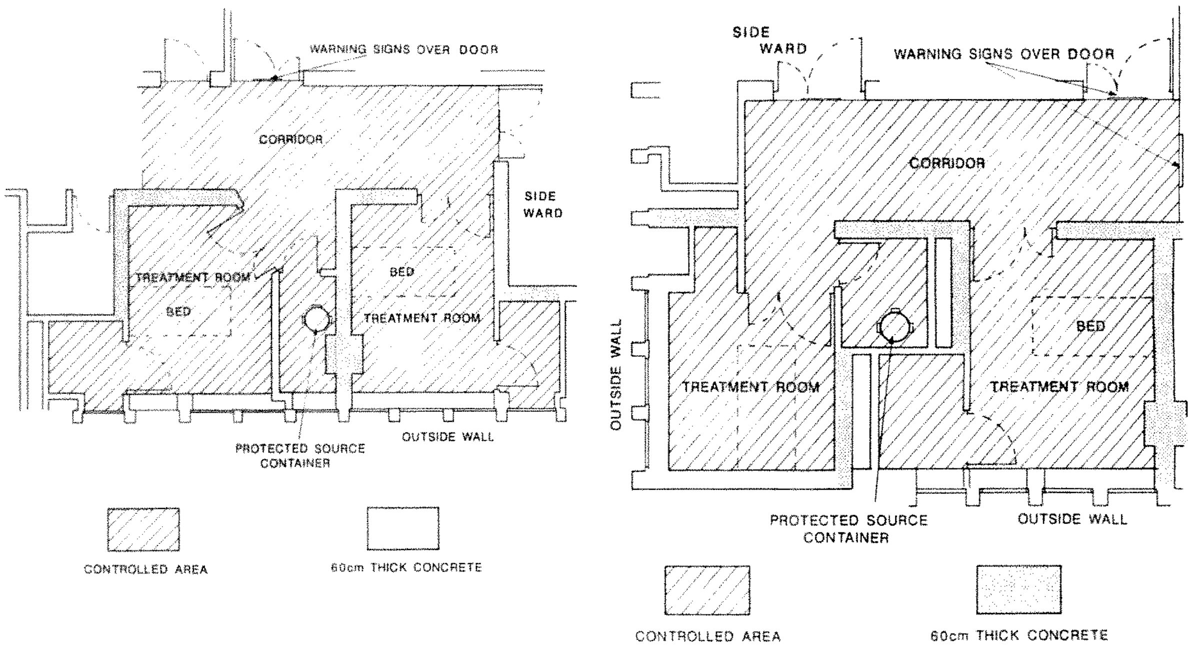
$$0.05 \times 0.132 \times 0.97 = 0.0064 \text{ man Sv.}$$

The implied cost of the reduction in collective dose equivalent resulting from the building of the mazes would therefore be

$$\text{£}(5\,500/0.0064) \text{ per man Sv}$$
$$= \text{£}860\,000 \text{ per man Sv.}$$

As this sum is substantially more than the £4 000 per man Sv for health detriment or the £50 000 per man Sv if nurses are considered as members of the public, and since mazes would have reduced the size of the rooms so that they would have become almost unusable, it was concluded that the construction of mazes was not justified. This decision meant that controlled areas would need to be created outside the doors to the rooms where the IDR would be in excess of 7.5 μSvh^{-1}, since it was not possible in the case of brachytherapy techniques, where treatment times usually exceed 8 h, to make use of the exemption in Schedule 6 of the IRR 85 relating to time-averaged dose rate (TADR).

When the Selectrons became operational, dose measurements were made outside the rooms to determine the extent of the controlled areas (Fig. 1). Whilst only the immediate area outside the entrance to the rooms needed to be controlled, it was decided, for operational reasons, to extend the controlled area to include the whole of the corridor. Local rules were produced and implemented which contained a system of work for all staff entering the controlled area as defined by a plan of the ward area (Fig. 2), and an operational policy for using the equipment. To comply with the ALARA principle, bed shields were used to reduce the IDR in these areas and also to reduce the dose to adjacent side wards owing to transmission through the doors. While bed shields are desirable, the maximum usable size is restricted by the weight and by the ease of carrying out nursing procedures using the shields. In our situation, the bed shield chosen measured 90 × 50 × 2.5 cm and weighed 130 kg. It must also be remembered that with a remote afterloading system the sources are automatically retracted into a safe position before staff enter the room. Bed shields therefore only have the effect of reducing the dose rate to people in the



(a) (b)

Figure 2. Bristol Radiotherapy Centre Selectron treatment suite: (a) Ward 61 and (b) Ward 62.

corridor and providing limited protection in the event of the sources failing. They are not required to provide protection when nursing procedures are being carried out; indeed, it is often necessary to move the bed shield to allow access to the patient prior to carrying out the procedures, *e.g.* when checking to ensure that the applicator has not moved.

Analysis of nursing staff dose records

Over the period from 1980 to 1987 there has been a marked reduction in collective dose to nursing staff on the two wards, as seen in Table I. During this period there have been changes in monitoring techniques, an increase in the number of qualified staff employed on the wards in 1984 as well as the introduction of MDR

Table I. Collective dose to nursing staff

Year	Number of monthly monitoring periods	Collective dose per year (man mSv)	Average dose per month (μSv)	Equivalent yearly average dose (mSv)
1980	455	145.0	318.7	3.82
1981	502	170.0	338.6	4.06
1982 (January–March)	133	34.4	258.6	3.10
1982 (April–December)	387	97.8	252.7	3.03
Total 1982	520	132.2	254.2	3.05
1983	525	89.5	170.5	2.05
1984	858	55.8	65.0	0.78
1985 (January–August)	460	50.6[a]	73.3	0.88
Selectrons operational from September 1985 to date				
1985 (September–December)	240	23.1[b]	32.1	0.39
1986	758	27.9	36.8	0.44
1987	875	25.2	28.8	0.35

[a] Derived from measured cumulative dose of 33.7 man mSv from January to August.

[b] Derived from measured cumulative dose of 7.7 man mSv from September to December.

Table II. "Treatment units" for different brachytherapy treatments

Techniques	Code	Typical activity (mg Ra eq)	Average time of insertion (h)	mg Ra eq h	Treatment units
Breast implant	A	20	96	2000	0.8
Tongue implant	B	15	168	2500	1.0
Surface mould	B	15	168	2500	1.0
Manual gynae	Man	100	30	3000	1.2
Selectron gynae	Aft	250	10	2500	1.0

Selectron afterloading systems and the reinforcing of good radiation nursing practice in line with the ALARA principle. Monthly monitoring of staff was initially carried out using NRPB film badges until March 1982 when thermoluminescent dosemeters were used instead. This change had a minimal effect in reducing the average dose per monitoring period and hence cumulative dose to ward staff. The increase in the number of staff involved in patient treatment is reflected in the number of monthly monitoring periods each year.

On the assumption that the cumulative dose to nursing staff is directly related to the product of the sealed source activities used and the length of time taken for treatment, the amount of sealed source therapy carried out each year has been determined in terms of a "treatment unit", where one treatment unit is equivalent to 2500 milligram radium equivalent hours (mg Ra eq h). Values of the treatment unit for different brachytherapy techniques are given in Table II. Using these values, the number of treatment units per annum have been determined and used to normalize the collective dose per annum and the average dose per month (see Table III). From this table, it can be seen that the collective dose per treatment unit appears to have changed following the review of the sealed source operational policy in mid-1983, as a result of which, staff were encouraged to comply with the ALARA principle and again following the introduction of the Selectrons for gynaecological treatments. The reduction in the collective dose per treatment unit attributable to the former and to the change in monitoring technique was about 35–40%, while the introduction of the MDR Selectrons caused further reduction in collective dose per treatment unit of about 70%, thereby giving an overall reduction of about 85%. Over the same period there was a reduction in the average monthly dose to nursing staff of about 90%. This can be attributed in part to implementation of the ALARA principle in nursing practice and the increase in the number of nursing staff as well as to the introduction of the two MDR afterloading systems.

Conclusions

The gradual enforcement of the ALARA principle from mid-1983 contributed to the reduction of dose to nursing staff as shown by the reduction in collective dose per treatment unit, whilst the increase in the number of nursing staff led to a reduction in the average dose per treatment unit. These, together with the introduction of remote afterloading systems in 1985, had the effect of reducing the average monthly dose to nursing staff by 85–90%.

Table III. Collective dose/year and average dose/month

Year	Number of implants		Number of gynae patients		Number of treatment units (2500 mg Ra eq h)	Collective dose/year/ treatment unit (man mSv/unit)	Average dose/month/ treatment unit (μSv/unit)
	A	B	Man	Aft			
1980	7	7	125	0	162.6	0.892	1.96
1981	6	13	172	0	224.2	0.758	1.51
1982	2	32	113	0	169.2	0.781	1.50
1983	7	21	127	0	179.0	0.500	0.955
1984	8	3	82	0	107.8	0.518	0.603
1985 To August 1985	1	13	53	0	77.4	0.435	0.631
From September 1985							
1985	1	10	12	18	43.2	0.103	0.248
1986	27	13	42	94	179.0	0.150	0.191
1987	36	12	6	103	151.0	0.167	0.191

The decision to adopt controlled areas and the consequent use of local rules, systems of work and operational policies rather than build mazes at the entrance to the treatment rooms has been justified in terms of lower staff doses even with areas of high instantaneous dose rate. This policy has resulted in the saving of the substantial sum of money which would have been required to carry out the necessary structural changes to reduce the TADR outside the entrances to the wards to less than 7.5 μSv h^{-1}.

References

CLARK, M. J., FLEISHMAN, A. B. & WEBB, G. A. M., 1981. Optimisation of the Radiological Protection of the Public. (A provisional framework for the application of cost-benefit analysis to normal operations.) NRPB—R120 (NRPB, Chilton, Oxford).

FLEISHMAN, A. B., NOTLEY, H. M. & WILKINSON, J. M., 1983. Cost benefit analysis of radiological protection: a case study of remote after-loading in gynaecological radiotherapy. *British Journal of Radiology, 56*, 737–744.

HUNTER, R. D., 1985. In *Brachytherapy 1984*, ed. by R. F. Mould (Nucletron Trading B.V., Holland).

IONISING RADIATION REGULATIONS (IRR 85), 1985. SI 1985 No. 1333 (HMSO, London).

NATIONAL RADIOLOGICAL PROTECTION BOARD (NRPB), 1982. *Cost-Benefit Analysis in the Optimisation of Protection of Radiation Workers. A Consultative Document. Report ASP4* (NRPB, Chilton, Oxford).

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Technical note

A sweet solution to a contrast problem

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Prior to a computed tomographic (CT) examination, it is our custom to sedate most children under the age of 4 years with oral chloral hydrate syrup. In children who have been fasted, sedated thus, and not given an oral contrast agent, we have noticed opacification of both gastric and duodenal lumena (Fig. 1). It was decided to investigate this phenomenon.

Method

The scans were performed on an Elscint 2400 at 120 kVP and 252 mA. The various constituents of the chloral hydrate syrup were scanned in plastic medicine cups atop a body phantom (Table I). The simple syrup result was confirmed by repeating the procedure with household granulated sugar dissolved in water. In each case the attenuation values were measured with a small "region of interest" marker. The value recorded is an average of five values from the centre of the object.

Following this, standard plastic disposable 50 ml syringes were scanned transversely, with the following contents: simple syrup, water and 3% gastrografin (Fig. 2). The window setting was that for a standard abdominal CT (W:350, C:0).

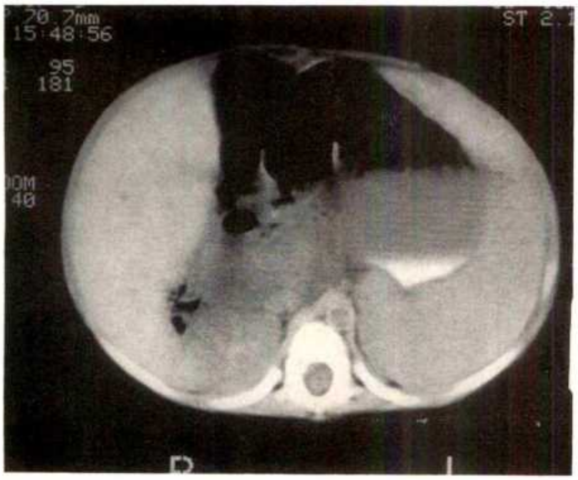

Figure 1. The opacification of gastric lumen following oral choral hydrate syrup.

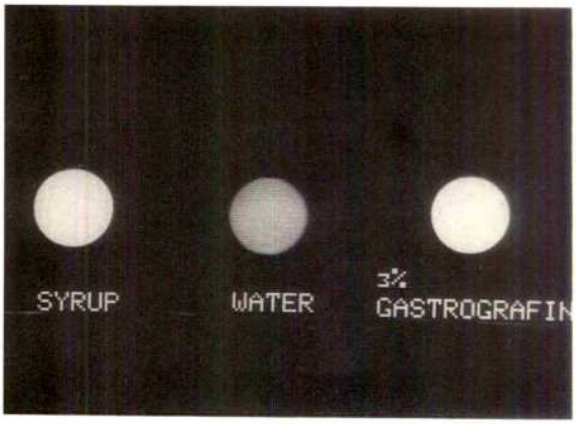

Figure 2. Transverse CT scans of syringes containing syrup, water and 3% gastrografin.

Discussion

The chloral hydrate syrup used in this hospital consists of simple syrup, chloral hydrate, raspberry flavouring and amaranth (colouring). Simple syrup constitutes 95% by volume of the mixture.

Syrup is used as a base for many unpleasant tasting medicines, and consists (simply) of sucrose 66% and water 34% w/w. It follows that an opaque gastric fluid may be found in any patient taking syrup-based medication whilst otherwise fasting for CT. This applies particularly to children, as the use of syrup-based medication in adults is unusual.

Table I. Scanned substances under investigation.

Test substance	Hounsfield units
Water	0
Gastrografin 3%	386
Chloral 60 mg/ml (in raspberry syrup)	377
Chloral 60 mg/ml (in distilled water)	64
Raspberry flavour	0
Amaranth	3
Simple syrup	351

The degree of attenuation produced is almost the same as that of 3% gastrografin, the usual oral contrast agent for abdominal CT in this hospital, and indistinguishable from it at W:350, C:0.

Knowledge of this property of simple syrup will avoid the possibility of an erroneous diagnosis of upper gastrointestinal haemorrhage. A question is raised as to whether an oral contrast agent for CT could be developed from a non-absorbable sugar which may be theoretically safer, and perhaps more palatable, than gastrografin.

Conclusion

Simple syrup (sucrose 66% and water 34% w/w) has been found to have the same radiation attenuation as 3% gastrografin on CT.

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Case reports

Giant mid-oesophageal diverticulum: a rare cause of dysphagia

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Mid-oesophageal diverticula are usually small, asymptomatic and rarely result in complications (Meshkinpour, 1985). We report a case of a giant mid-oesophageal diverticulum which caused dysphagia. The aetiology of these diverticula is discussed.

Case report

A 91-year-old man presented with a long history of dysphagia and weight loss of over 20 kg. More recently he had developed vomiting and symptoms of nocturnal aspiration. The dysphagia had become severe and he required intravenous fluids to maintain his hydration.

The chest radiograph demonstrated an irregular gas lucency inferior to the carina (Fig. 1). There was no evidence of previous tuberculous infection. Barium swallow examination revealed a huge sac arising from the mid-part of the oesophagus and extending to the left and anterior to it. Initially, the sac appeared thick walled (Fig. 2), but on delayed radiographs barium penetrated the food residue within it revealing a thin walled diverticulum. Barium preferentially entered the diverticulum, then overflowed into the distal oesophagus which was displaced by the diverticulum and demonstrated non-propulsive contractions.

Endoscopy confirmed the radiological findings of a large mid-oesophageal diverticulum. The distal oesophagus was macroscopically normal and the endoscope passed readily into the stomach. He was not willing to undergo oesophageal manometry. Surgery was also refused so he was fed enterally via a nasogastric tube.

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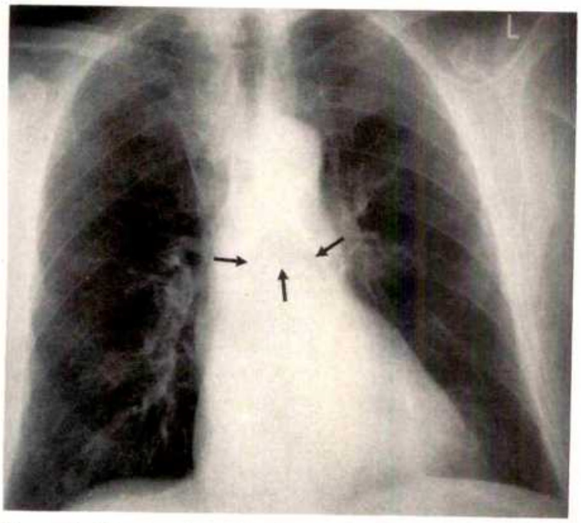

Figure 1. Chest radiograph demonstrating an irregular gas lucency in the mediastinum (arrows).

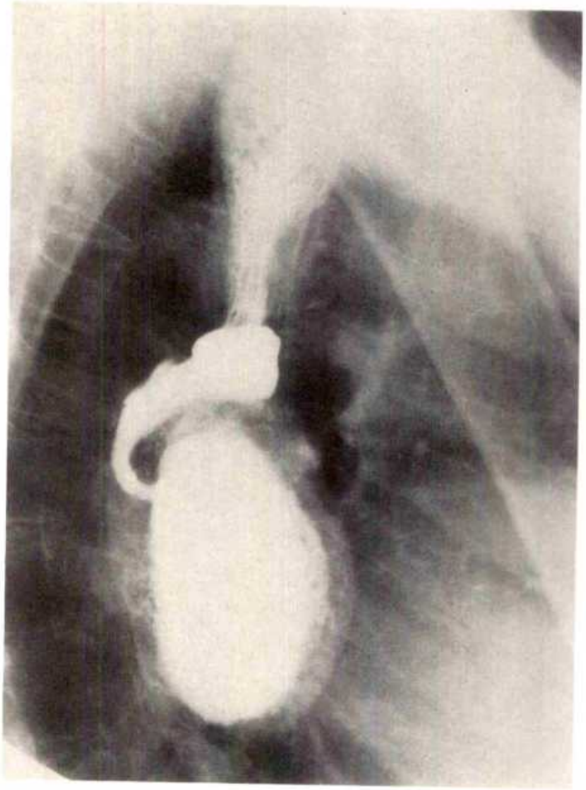

Figure 2. Early lateral film from barium swallow showing contrast medium entering the diverticulum.

Discussion

Oesophageal diverticula may be classified anatomically as pharyngo-oesophageal, mid-oesophageal, intramural and epiphrenic. Classification into traction and pulsion on the basis of the presumed aetiology was first suggested by Rokitansky in 1840 (from Meshkinpour, 1985).

Mid-oesophageal diverticula are widely thought to be of traction origin; this is based on early observations of an association between tuberculous lymph nodes and diverticula of the adjacent oesophagus. Although diverticula are associated with other causes of mediastinal fibrosis such as treated non-Hodgkin's lymphoma (Barosi et al, 1976) and histoplasmosis (Jenkins et al, 1976), post-mortem studies have failed to demonstrate fibrous adhesions in most cases suggesting that traction is the cause in only a minority.

It has also been suggested that oesophageal motility disorders may result in mid-oesophageal diverticula. Kaye (1974) found manometric evidence of significant oesophageal motor dysfunction in 10 out of 12 patients. Similarly, Borrie and Wilson (1980) found motor abnormalities in four of five cases. Other potential explanations include a congenital origin (Borrie & Wilson, 1980) or pseudo-diverticulum due to a walled-off perforation.

Mid-oesophageal diverticula are rarely symptomatic (Jordan, 1977; Meshkinpour, 1985) since they are generally small, have wide necks and the sac is usually higher than the neck of the diverticulum, preventing the retention of food (Meshkinpour, 1985).

Our case is unusual because the diverticulum was symptomatic. This may be partly a result of its large size causing oesophageal displacement. In addition, the position of the sac predominantly below the level of its neck resulted in preferential filling of the diverticulum.

The aetiology of this diverticulum is unclear; although formal manometric studies could not be performed the uncoordinated distal oesophageal contractions did not delay the passage of barium, so they may be clinically insignificant. There was no evidence of previous tuberculosis and no history to suggest previous oesophageal perforation.

A mid-oesophageal diverticulum should be considered in the differential diagnosis of dysphagia, and as a cause of an abnormal gas collection in the middle mediastinum on plain radiographs. Barium swallow readily confirms the diagnosis.

References

Barosi, G., Morandi, S. & Ascari, E., 1976. On a case of esophagus involvement by non-Hodgkin's lymphoma. Remission by chemotherapy alone. *Hematologica*, *61*, 219–223.

Borrie, J. & Wilson R. L. K., 1980. Oesophageal diverticula: principles of management and appraisal of classification. *Thorax*, *35*, 759–767.

Jenkins, D. W., Fisk, D. E. & Byrd, R. B., 1976. Mediastinal histoplasmosis with esophageal abscess. *Gastroenterology*, *70*, 109–111.

Jordan, P. H., 1977. Dysphagia and esophageal diverticula. *Postgraduate Medicine*, *61*, 155–161.

Kaye, M. D., 1974. Oesophageal motor dysfunction in patients with diverticula of the mid-thoracic oesophagus. *Thorax*, *29*, 666–672.

Meshkinpour, H., 1985. Esophageal diverticula. In *Bockus Gastroenterology*, *4th edn*, *Vol. 2*, ed. by J. Edward Berk (W. B. Saunders Company, Philadelphia, USA), pp. 809–817.

The use of combined transoesophageal echocardiography and fluroscopy in the biopsy of a right atrial mass

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Transoesophageal echocardiography has increasing application to the diagnosis of a wide range of cardiac disorders (Roelandt & Sutherland, 1988). Recently, simultaneous ultrasound imaging of the heart by the oesophageal route has been used during certain interventional cardiac procedures (Cryan et al, 1988; Neumann et al, 1988).

We report a case in which transoesophageal echocardiography was used in combination with fluroscopy to facilitate the biopsy of a right atrial mass.

Case report

A 14-year-old Asian boy presented with a short history of malaise, cough and haemoptysis associated with intermittent pleuritic chest pain. Physical examination revealed signs of bilateral pleural effusions and right-sided heart failure, with jugular venous pressure elevated 6 cm above the suprasternal notch and mild peripheral oedema. His pulse rate was 90 beats/min and his blood pressure was 140/80 mmHg with no paradox. The pleural effusions were confirmed radiologically, but the chest radiograph and electrocardiogram (ECG) yielded no further diagnostic information. Pulmonary infarcts were suspected and, in the search for a source of emboli, praecordial cardiac ultrasound revealed distortion of the tricuspid valve annulus. This was further delineated by transoesophageal echocardiography which clearly showed a mass in the posterolateral

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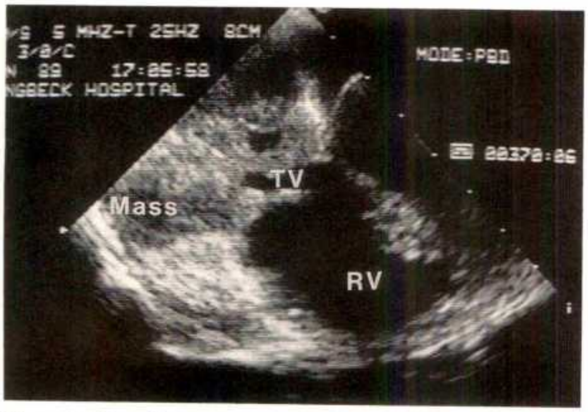

Figure 1. Two-dimensional transoesophageal echocardiogram demonstrating the large mass in the wall of the right atrium and causing distortion of the tricuspid valve. RV = right ventricle and TV = tricuspid valve.

wall of the right atrium causing displacement of the tricuspid valve (Fig. 1).

The patient's family were unwilling to allow cardiac surgery to be performed and so a biopsy of the mass was chosen as the next diagnostic approach. A Cordis bioptome was introduced via the right femoral vein and tip positioned at the junction of the inferior vena cava and the right atrium using radiological screening. From this position the jaws of the bioptome were manoeuvred accurately into the centre of the mass, and away from the free wall of the atrium, guided by simultaneous transoesophageal echocardiography (Figs. 2 and 3). The procedure was repeated several times to provide sufficient samples for histological and microbiological examination.

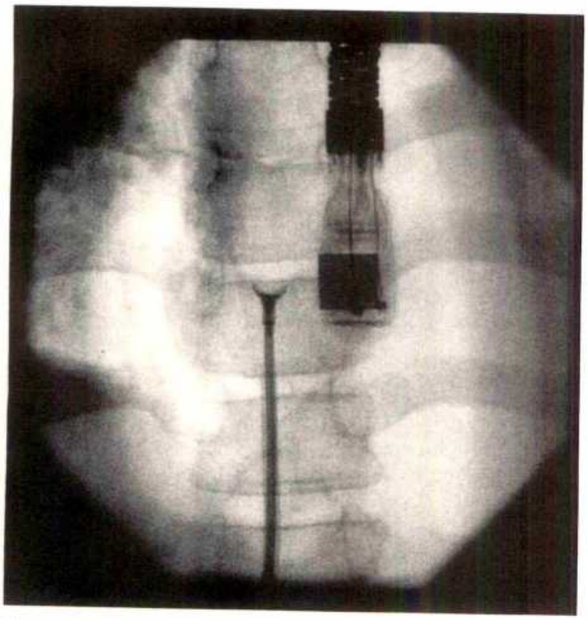

Figure 2. Radiograph showing the orientation of the transoesophageal ultrasound probe to the bioptome during biopsy of the mass.

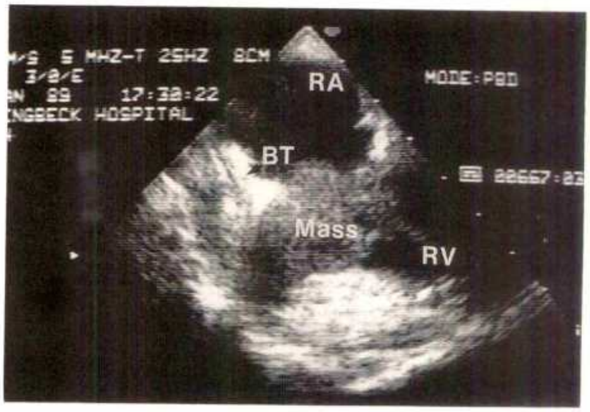

Figure 3. Two-dimensional transoesophageal echocardiogram during the biopsy procedure showing the tip of the bioptome entering the mass. BT = bioptome, RA = right atrium and RV = right ventricle.

Discussion

Cardiac biopsy is usually performed from the right ventricle to diagnose and manage a wide range of myocardial disorders (Fowles & Mason, 1984), and using a transvenous route the complication rate is around 1% (Sekiguchi & Take, 1980). The major cause of morbidity and mortality is cardiac perforation with resultant cardiac tamponade. When comtemplating biopsy within the thin-walled right atrium, the chances of perforation would be considered more likely. In our patient the mass was situated on the free (posterolateral) wall of the right atrium, therefore making blind biopsy a potentially hazardous undertaking.

Transoesophageal echocardiography gives high quality cardiac images (Schluter et al, 1982) and has been used in the diagnosis of both intracardiac and extracardiac masses (Nellessen et al, 1986). It has recently been performed during interventional cardiac procedures, to guide balloon placement and to assess the success of balloon aortic valvuloplasty (Cryan et al, 1988), and also reported is its use during extraction of an embolized central venous catheter tip (Neumann et al, 1988). Whilst praecordial cardiac ultrasound has been used during endomyocardial biopsy (di Pennestri et al, 1982), to the authors' knowledge this is the first description of the use of transoesophageal echocardiography to guide intracardiac biopsy. In our patient, the clarity of the ultrasound images obtained by the oesophagel route made it possible to guide the tip of the biopsy forceps into the mass, thus avoiding any chance of perforating the atrial wall. We would recommend its use in similar situations.

Acknowledgments

Drs Scott and Ettles are supported by the National Heart Research Fund.

References

Cryan, S. E., Kimball, T. R., Schwartz, D. C., Meyer, R. A., Steed, R. D. & Kaplan, S., 1988. Evaluation of

1990, *The British Journal of Radiology*, *63*, 224–226 Case report

balloon aortic valvuloplasty with transoesophageal echocardiography. *American Heart Journal*, *115*, 460–462.

Fowles, R. E. & Mason, J. W., 1984. Role of cardiac biopsy in the diagnosis and management of cardiac disease. *Progress in Cardiovascular Diseases*, *27*, 153–172.

Nellessen, U., Daniel, W. G. & Lichtlen, P. R., 1986. The diagnostic value of transoesophageal echocardiography in the detection of cardiac and extracardiac masses. *Zeitschrift für Kardiologie*, *75*, 91–98.

Neumann, H. P. H., Hofmann, T., Koester, W., Billmann, P. & Kauffmann, G. W., 1988. Extraction of an intracardiac catheter embolus using combined radiography and transoesophageal echocardiography. *Clinical Cardiology*, *11*, 427–429.

di Pennestri, F., Loperfido, F., Salvatori, M. P., Mongiardo, R., Mazzari, M., Montenero, A. S. & Coppola, E., 1982. L'eco 2D nella guida all'esecuzione della biopsia miocardica. *Cardiologia*, *27*, 1141–1145.

Roelandt, J. R. I. C. & Sutherland, G. R., 1988. Oesophageal echocardiography. (Editorial) *British Heart Journal*, *60*, 1–3.

Schluter, M., Langenstein, B. A., Polster, J., Kremer, P., Souquet, J., Engel, S. & Hanrath, P., 1982. Transoesophageal cross-sectional echocardiography with a phased array transducer system. Technique and initial clinical results. *British Heart Journal*, *48*, 67–72.

Sekiguchi, M. & Take, M., 1980. World survey of catheter biopsy of the heart. In *Cardiomyopathy: Clinical, Pathological and Theoretical Aspects*, ed. by M. Sekiguchi and M. Take (University Park Press, Baltimore and University of Tokyo Press, Tokyo), pp. 217–225.

Iliopsoas abscess: an unusual complication of femoral artery catheterization

By E. J. Loveday, MRCP, K. A. Tonge, FRCR and *H. G. du Peloux Menage, BSc, MRCP

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(Received July 1989)

We report a case of iliopsoas abscess following percutaneous transfemoral carotid angiography. To our knowledge there are no previous reports of this complication.

Case report

The patient, a woman aged 49, was admitted for investigation of occlusive cerebrovascular disease. She was a smoker and had a history of exopthalmic Graves' disease and thyrotoxicosis, previously treated with Iodine 131. Current medications were thyroxine, Voltarol Retard and Nifedipine Retard. Prior to the procedure, haemoglobin level was 14.2 g/dl, white cell count was 8400×10^3/ml and platelet count was $283\,000 \times 10^3$/ml. Full clotting studies were normal.

Carotid arteriography was performed using a modified Seldinger technique. Full aseptic precautions were taken including groin shave, cleansing with chlorhexidine, povidone iodine skin preparation and sterile drapes and gowns. A 5 F Mani catheter (William Cook Europe ApS) and a 0.035 inch straight guidewire were used during the procedure which was protracted owing to inability to catheterize the left common carotid artery. A subsequent arteriogram using a 5 F pigtail catheter revealed complete occlusion of this vessel at its origin. Compression was applied to the puncture site for 20 min. The patient was well following the procedure and was discharged home shortly thereafter. Minor bruising only was seen at the puncture site.

She presented again 22 days post-investigation complaining of increasing pain in the right groin and difficulty with walking. On examination she was pyrexial; and greenish, offensive smelling fluid was oozing from the puncture site in the right groin. There was a 30° fixed flexion deformity of the right hip, and any attempt to straighten the leg resulted in severe pain. Haemoglobin concentration had fallen to 10.5 g/dl and the white cell count had risen to $21\,000 \times 10^3$/ml. A computed tomographic (CT) scan of the abdomen and pelvis was performed, and this confirmed the clinical diagnosis of a retroperitoneal abscess involving the iliopsoas muscles, with extension down into the groin, posterior to the femoral vessels (Fig. 1). An intravenous digital subtraction angiography examination showed no abnormality of the iliac or femoral arteries and no impairment of the arterial supply to the legs. Wound swabs from the puncture site grew *Staphylococcus aureus*.

At operation a large loculated retroperitoneal abscess was found and this was subsequently drained. Culture of the abscess fluid also grew *Staphylococcus aureus* with the same spectrum of antibiotic sensitivity as that previously isolated. The patient made an uneventful recovery and was well at follow-up 3 months later.

Discussion

Chronic colonization by *Staphyloccocus* and other pathogens in the inguinal skin is well described (Szilogyi et al, 1972), but the degree of bacterial contamination required to cause a wound infection in healthy tissues is very high; however, a relatively low level may suffice in the presence of tissue trauma and haematoma (Burke, 1961). Indeed, tissue trauma, haematoma formation and possible bacterial contamination introduced at the time of percutaneous transfemoral arteriography have been implicated in an increased incidence of post-operative wound infection following arterial bypass surgery if the

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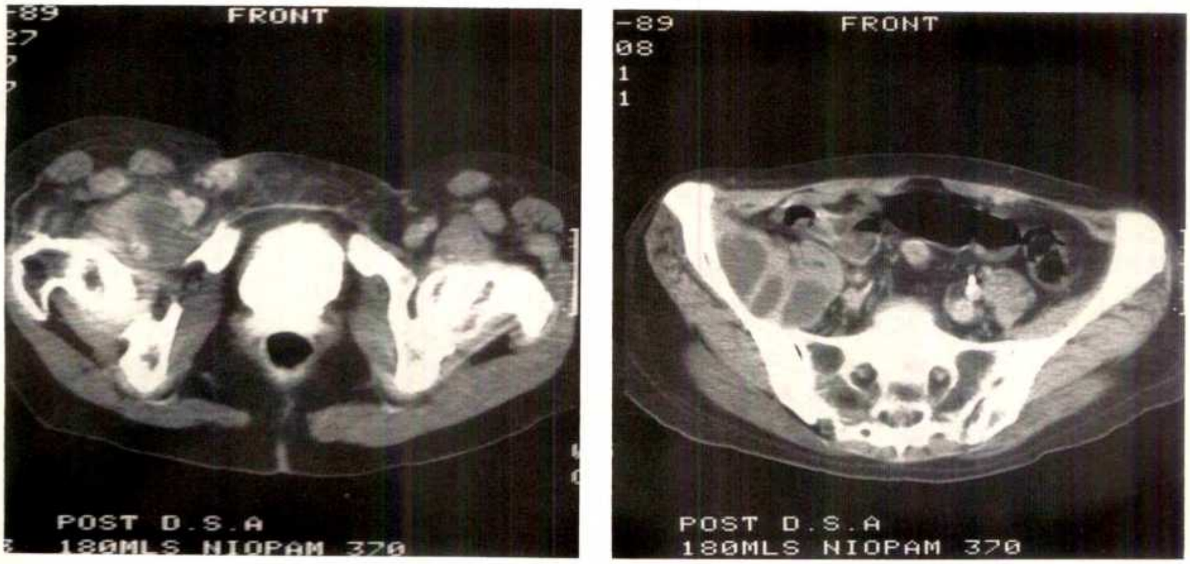

(a) (b)

Figure 1. CT scans following intravenous contrast enhancement. (a) The section near the puncture site shows a soft-tissue mass posterior to the groin vessels involving the iliopsoas muscle close to its insertion and (b) the extension of the infective process is shown proximally, confined by the iliopsoas sheath, with multiple loculations.

same site was used for the pre-operative arteriogram (Landrenau & Raju, 1981).

Although bacterial contamination of catheters and guidewires may be relatively common (Shawker et al, 1974), clinical infection following angiography is surprisingly rare (Herlinger, 1976). To our knowledge iliopsoas abscess has not previously been reported following femoral artery catheterization, although three cases of retroperitoneal sepsis following translumbar aortography were reported in one large series of 13 207 cases (McAfee, 1957), Sutton (1962) described a case of infection of a groin haematoma following carotid arteriography, and more recently a case of septic arthritis of the hip has been ascribed to the preceding arteriogram (Resnik et al, 1987). Seven cases of huge retroperitoneal haematoma formation following Seldinger catheterization were reported in a series of 11 402 patients (Lang, 1963) and it is unsurprising therefore that infection of the same space might occur.

In our case the length of the procedure (approximately 60 min) and the need for a catheter change without use of a sheath may have contributed to tissue trauma and bacterial contamination, despite full aseptic precautions and adequate compression of the puncture site following the procedure. There was no evidence of immunological incompetence in our patient, nor any predisposing factors to retroperitoneal sepsis. A standard double-wall puncture technique was used: this may have permitted access for organisms to beneath the underlying strong iliopsoas fascia, which provides a pathway for extension of the infective process proximally into the retroperitoneal space (Myers, 1982).

Although infection following angiography is extremely rare, the consequences may be severe, as in our case, although our patient fortunately made a full recovery. This case report is intended to alert radiologists and clinicians to the possibility of retroperitoneal sepsis following percutaneous transfemoral arterial catheterization, and emphasizes the need for scrupulous aseptic technique during these procedures.

Acknowledgments

We thank Dr R. Ross-Russell for his help in allowing us to report his patient.

References

BURKE, J. F., 1961. The effective period of preventive antibiotic action in experimental skin incisions and dermal lesions. *Surgery*, *50*, 161–168.

HERLINGER, G., 1976. Aortography and peripheral arteriography. In *Complications in Diagnostic Radiology*, ed. by G. Ansell (Blackwell Scientific, Oxford), pp. 42–75.

LANDRENAU, M. D. & RAJU, S., 1981. Infections after elective bypass surgery for lower limb ischaemia: the influence of preoperative transcutaneous arteriography. *Surgery*, *90*, 956–961.

LANG, E. K., 1963. A survey of the complications of percutaneous retrograde arteriography, Seldinger technic. *Radiology*, *81*, 257–263.

MCAFEE, J. G., 1957. A survey of complications of abdominal aortography. *Radiology*, *68*, 825–838.

MYERS, M. A., 1982. *Dynamic Radiology of the Abdomen* (Springer-Verlag, New York), p. 181.

RESNIK, C. S., SAWYER, R. W. & TISNADO, J., 1987. Septic arthritis of the hip: a rare complication of angiography.

Journal of the Canadian Association of Radiologists, *38*, 299–301.

SHAWKER, T. H., KLUGE, R. M. & AYELLA, R. J., 1974. Bacteremia associated with angiography. *Journal of the American Medical Association*, *229*, 1090–1092.

SUTTON, D., 1962. *Arteriography* (E. S. Livingstone, London), p. 54.

SZILOGYI, D. E., SMITH, R. F., ELLIOTT, J. P. & VRANDECIC, M. P., 1972. Infection in arterial reconstruction with synthetic grafts. *Annals of Surgery*, *176*, 321–333.

1990, *The British Journal of Radiology*, 63, 227–228

Case of the month

The case of the surplus clues

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(*Received March 1989*)

A 16-year-old girl was admitted with a history of backache, fever and 4 month history of generalized weakness. Examination revealed pallor, sternal tenderness and hepatomegaly. Urine examination and the blood biochemistry were essentially normal. The haematological examination showed: haemoglobin, 5.5 gm%; packed cell volume, 16%; reticulocyte count, 2%; platelet count, 4000 cm^3; total leucocytic count, 9800 cm^3; and differential leucocytic count: 40% segmental neutrophils, 30% bands, 16% lymphocytes, 10% monocytes and 4% lymphoblasts with deeply basophilic cytoplasm containing prominent vacuoles. Subsequently, radiographs of the chest (Fig. 1), dorsolumbar spine (Fig. 2), skull (Fig. 3) and pelvis (Fig. 4) were obtained. What is your differential diagnosis?

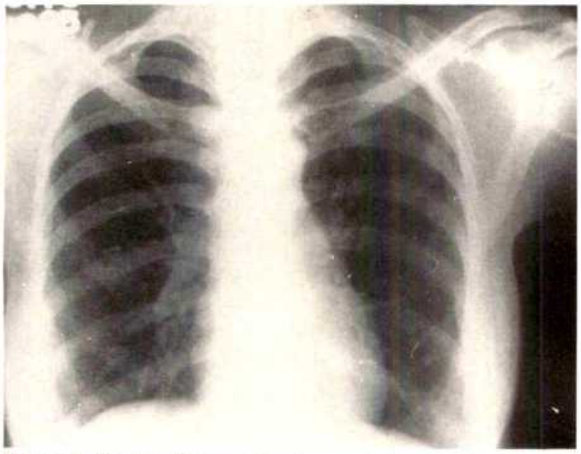

Figure 1. Chest radiograph (postero-anterior view).

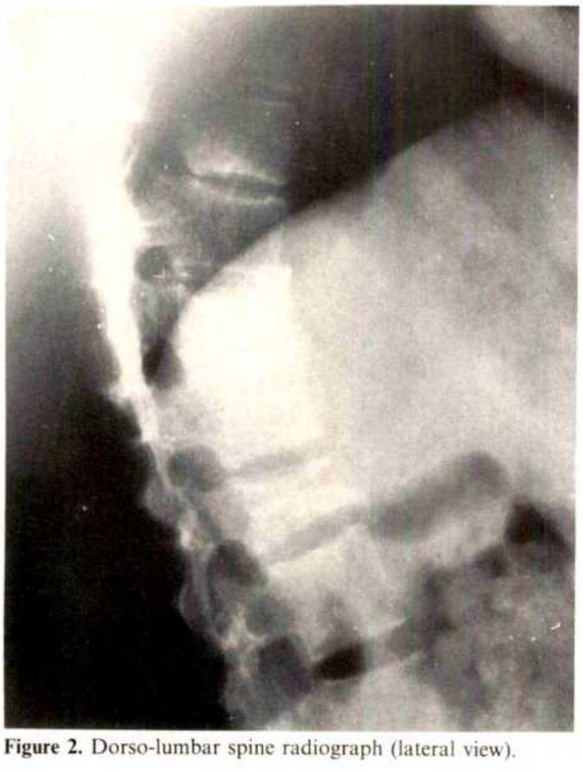

Figure 2. Dorso-lumbar spine radiograph (lateral view).

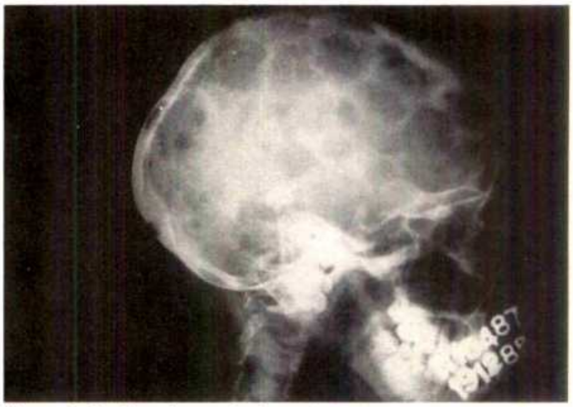

Figure 3. Skull radiograph (lateral view).

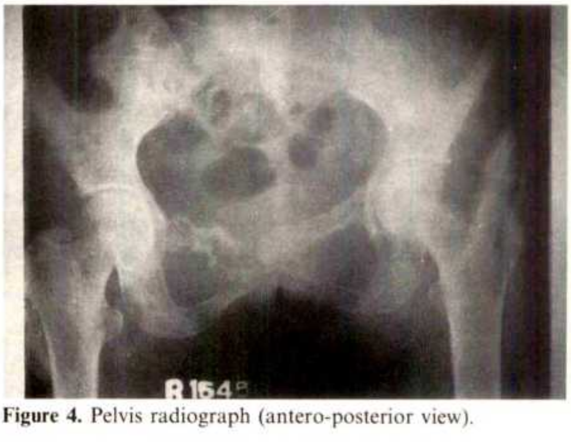

Figure 4. Pelvis radiograph (antero-posterior view).

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The chest radiograph (Fig. 1) showed a few ill-defined osteolytic lesions involving the lateral end of the left clavicle and left scapula. There were vertebral collapses involving the first and third lumbar vertebrae with intact disc spaces (Fig. 2). The radiograph of the skull showed widespread destructive lesions involving the vault (Fig. 3) and the radiograph of the pelvis showed expansile destructive lesions involving the pubic bones (Fig. 4). Serum calcium and phosphorus levels were within normal limits and serum alkaline phosphatase was mildly elevated. The radiological differential diagnosis of such skeletal lesions usually includes lymphoma, metastatic deposits, histiocytosis-X, cystic tuberculosis, cystic angiomatosis and hyperparathyroidism (Wilner, 1982). Skeletal involvement secondary to acute leukaemia is unlikely in view of the pattern and extent of radiological involvement.

The lymphoblasts in the peripheral smear showed typical features of Burkitt's cells. Bone marrow examination revealed 60% infiltration by these polyvacuolated blast cells. Histochemical stains for Sudan Black, Peroxidase and Periodic Acid Schiff were negative, whereas there was a positive reaction with Oil Red. The diagnosis of L-3 acute lymphoblastic leukaemia (acute leukaemia with Burkitt-type cells) was thus established (Bennet et al, 1976). The patient was treated with chemotherapy and radiotherapy and remained in remission for 14 months, then she had a relapse and died.

A rare variant among acute leukaemias, L-3 acute lymphoblastic leukaemia is a specific disorder accounting for 1–3% of all acute lymphoblastic leukaemia (ALL) patients (Schaeffer et al, 1984; Mangan et al, 1985). Clinical differentiation of L-3 ALL from other forms of ALL is usually not possible, except that the former runs a more aggressive course and is usually fatal within 6 months (Flandrin et al, 1975). The leukaemic blast cells in these patients are, however, readily recognized by the characteristic cytological and immunological features (Mangan et al, 1985). It is important to differentiate L-3 ALL from Burkitt's lymphoma, in which the patients usually present with characteristic extranodal tumour masses involving the jaws or the abdominal viscera. These patients of Burkitt's lymphoma can occasionally develop a leukaemic picture in the terminal stages.

Radiological involvement in L-3 ALL has received little attention (Flandrin et al, 1975; Marmary et al, 1981). Flandrin et al reported isolated lytic lesions in the humerus (one patient), tibia (one patient) and mandible (one patient). Marmary et al described a patient of L-3 ALL with diffuse demineralization and numerous osteolytic lesions in the mandible. The widespread and extensive skeletal destruction seen in this patient has not previously been reported. We wish to emphasize that L-3 ALL, although rare, should also be considered in the radiological differential diagnosis of widespread, destructive skeletal lesions.

Acknowledgment

We acknowledge the help of Dr T. K. Basu (haematologist, Safdarjang Hospital) in preparing this manuscript.

References

BENNETT, J. M., CATOVSKY, D., DANIEL, M. T., FLANDRIN, G., GALTON, D. A. G., GRALNICK, H. R. & SULTAN, C., 1976. Proposals for the classification of acute leukaemias. *British Journal of Haematology, 33*, 451–458.

FLANDRIN, G., BROUET, J. C. & DANIEL, M. T., 1975. Acute leukaemia with Burkitt's cells. A study of six cases with special reference to lymphocyte surface markers. *Blood, 45*, 183–189.

MANGAN, K. F., RANCH, A. E., BISHOP, M., SPIERS, A. S. O., LORCH, C. & SCHARFMAN, W. B., 1985. Acute lymphoblastic leukaemia of Burkitt's type (L-3 ALL) lacking surface immunoglobin and 8:14 translocation. *American Journal of Clinical Pathology, 83*, 121–126.

MARMARY, G., GERFUNKEL, A. & NAPARSTEK, E., 1981. Burkitt's lymphoma cell leukaemia. Radiology and cytotoxic medication. *International Journal of Oral Surgery, 10*, 367–370.

SCHLAEFFER, F., ZIBERMAN, D., HATSKELSON, L., KAPLAN, H. & VERMIQHU, T., 1984. Burkitt's-like acute lymphoblastic leukaemia—presentation of an unusual case: clinical features and diagnostic criteria. *Acta Haematologica, 72*, 45–48.

WILNER, D., 1982. *Radiology of bone tumours and allied disorders, Vol. II*, (W. B. Saunders & Company, Philadelphia) p. 1388.

1990, *The British Journal of Radiology*, *63*, 229–231

Correspondence

(The Editors do not hold themselves responsible for opinions expressed by correspondents)

A real headache!

THE EDITOR—SIR,

Drs Jackson and O'Donnell (1989) provided a useful review of intracranial arachnoid cysts when reporting their case which was associated with a contralateral chronic subdural haematoma. Radiologists should be able to recognize such cysts with confidence because they will find that their clinical colleagues are often unfamiliar with this rare lesion.

But the authors should not have omitted to mention subdural empyema as a possible cause of the contralateral surface collection. Patients with intracranial sepsis are usually acutely ill and in most cases the clinical picture suggests this diagnosis. However, if reliance is placed purely on pattern recognition, a computed tomographic (CT) distinction between pus and blood may not be possible. Linear surface enhancement is not usually a feature of uninfected subdural haematomas, and the presence of a membrane or "rim" on the medial side of the collection should always raise the possibility of sepsis (Burrows, 1985). Most empyemas are covered by thick and vividly enhancing membranes and most haematomas by no more than a thin rim caused by mechanical stasis of the iodine in the compressed cortical vessels. With non-acute extradural haematomas, a rare entity, the visible lentiform rim possesses, as might be expected, the same thickness and density as the falx (Fig. 1).

Yours etc.,
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(*Received October 1989*)

(*Author's reply*)

THE EDITOR—SIR,

Dr Burrows makes a good point regarding the differential diagnosis of an extradural collection with a linear enhancing rim. As he rightly points out, mistaken radiological diagnoses may be made if the clinical history is not taken into account. Our patient, as we stated, was asymptomatic and therefore a subdural empyema was not considered.

However, without any clinical details, we agree that this should be included in the differential diagnosis.

We thank Dr Burrows for his interest in our paper and for his helpful comments.

Yours, etc.,
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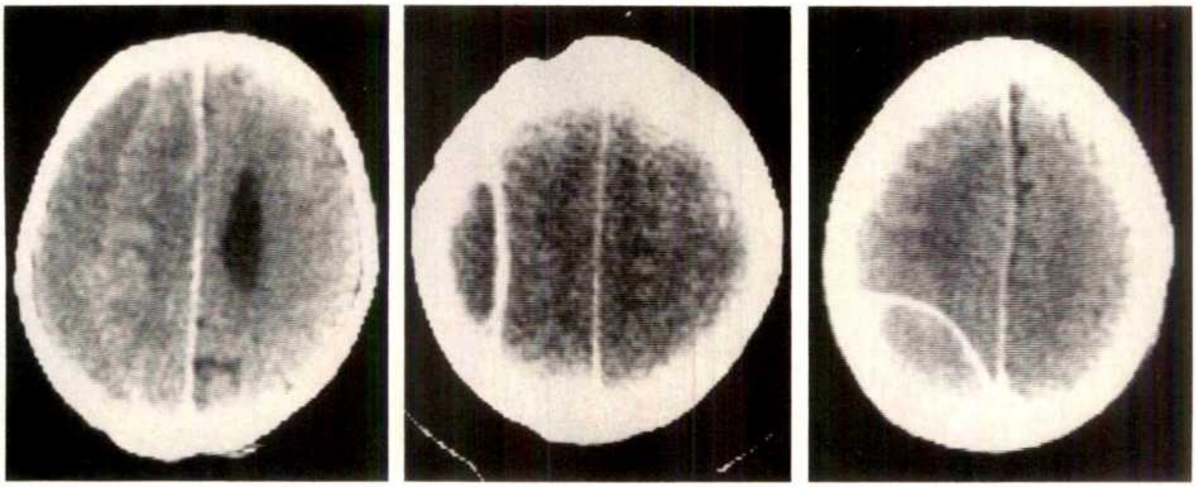
(*Received November 1989*)

References

BURROWS, E. H., 1985. Surface enhancement of the brain. *Clinical Radiology*, *36*, 233–239.

JACKSON, J. E. & O'DONNELL, C. J., 1989. A real headache! (Case of the month). *The British Journal of Radiology*, *62*, 867–868.



(a) (b) (c)

Figure 1. Enhanced brain CT slices in three different patients, each showing a different thickness and density of the overlying membrane. (a) Chronic subdural haematoma, (b) subdural empyema and (c) sub-acute extradural haematoma.

Conversion coefficients from fluence and air kerma to dose equivalent quantities

THE EDITOR—SIR,

Following the publication of the International Commission on Radiation Units and Measurements Report 39 (ICRU, 1985), the British Committee on Radiation Units and Measurements issued a memorandum (BCRU, 1986) recommending the adoption of the quantities ambient dose equivalent $H^*(d)$ and directional dose equivalent $H'(d)$ for area monitoring in the UK, and conversion coefficients and conversion relationships from fluence and air kerma to these quantities were given in an appendix. The promulgation of these conversion coefficients was in advance of any specific recommendation on conversion coefficients by the ICRU. The BCRU undertook to review the situation following any subsequent recommendations by the ICRU.

The ICRU Report 43 (ICRU, 1988) is now available and contains data on the same conversion coefficients, mainly in graphical form. The data for photons and neutrons is identical to that already recommended (BCRU, 1986). In the case of electrons, however, the BCRU memorandum gave a single mean value for the conversion coefficient for electron fluence to ambient dose equivalent $H^*(10)$ in the energy range 5 MeV to 50 MeV, whereas ICRU Report 43 contains more detail, tabulating conversion coefficients to both ambient and directional dose equivalent in the energy range 4 MeV to 21.4 MeV.

Since the publication of the BCRU 1986 memorandum, Publication 51 of the International Commission on Radiological Protection (ICRP, 1987) has also provided similar conversion coefficients. In the case of photons there is some divergence between the ICRU and the ICRP data, particularly at energies near 15 keV. However it has been shown (Böhm and Grosswendt, 1989) that for a range of X-ray spectra, weighted conversion coefficients from air kerma to $H'(10)$ or $H^*(10)$ are significantly different only for spectra with maximum photon energies of 20 keV and below when either the ICRU or ICRP data are used. For neutrons at energies where the ICRU and ICRP data may be compared, divergencies in the coefficients of $H^*(10)/\Phi$ of up to 9% are apparent. The data for electrons in ICRP Publication 51 refers to a 30 cm thick semi-infinite slab phantom rather than to the ICRU sphere.

On the basis of a recent review of the ICRU and ICRP publications, the BCRU now recommends that in the United Kingdom, for the conversion from fluence and air kerma to dose equivalent quantities,

(1) for photons and neutrons, the conversion coefficients and conversion relationships contained in the BCRU 1986 memorandum should continue to be used; these conversion coefficients are identical to those presented in ICRU 43 and

(2) for electrons, the conversion coefficients contained in ICRU 43 should be used and not the single mean value previously recommended (BCRU, 1986).

Yours etc.,
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References

BCRU, 1986. New quantities in radiation protection and conversion coefficients. *British Journal of Radiology*, *59*, 946–950.

BÖHM, J. & GROSSWENDT, B., 1989. 10 years of intercomparison measurements of dosemeter systems for the individual monitoring of photon and beta radiation. *PTB Mitteilungen*, *99*, 107–118.

ICRP, 1987. *Data for use in Protection Against External Radiation, ICRP Publication 51* (Pergamon Press, Oxford).

ICRU, 1985. *Determination of Dose Equivalents Resulting from External Radiation Sources, ICRU Report 39* (International Commission on Radiation Units and Measurements, Bethesda, MD).

ICRU, 1988. *Determination of Dose Equivalents from External Radiation Sources—Part 2, ICRU Report 43* (International Commission on Radiation Units and Measurements, Bethesda, MD).

Reactions to intravenous contrast media

THE EDITOR—SIR,

Idiosyncratic reactions are a recognized and documented complication of intravenous contrast media. Angioneurotic oedema is a relatively common feature of both intermediate (9%) and severe (16%) contrast media reactions. (Ansell, 1987). Typically, it involves the eyelids, lips, tongue and, in

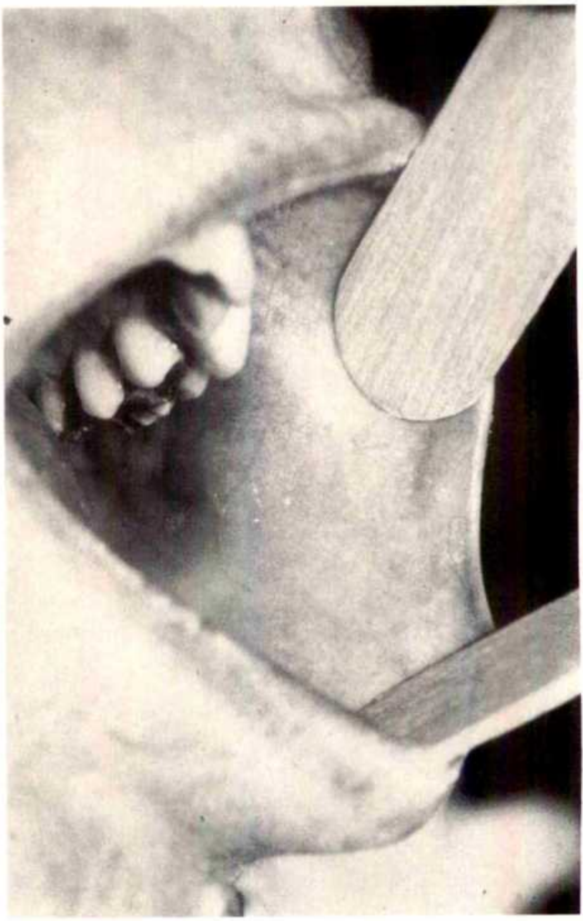

Figure 1. Open mouth view demonstrating the oedematous buccal mucosa.

more severe cases, the larynx. We recently encountered a case of angioneurotic oedema following intravenous contrast medium resulting in an unusual distribution of swelling.

A 52-year-old woman with known renal calculi was admitted with a history of left ureteric colic. Contrast medium (presumed to be high osmolar ionic) had been administered previously for intravenous urography without any adverse reaction. There was no history of allergy, asthma, eczema, diabetes, renal failure or cardiac disease. Biochemical renal function was normal. An intravenous urogram was performed using a bolus of 100 ml of sodium meglumine diatrizoate (Urografin 370, Schering), equivalent to 0.4 g iodine/kg. Within a few minutes the patient complained of facial discomfort and was noted to have facial flushing and significant swelling of her cheeks. Inspection of the inside of the mouth revealed that there was also marked bilateral oedema of the buccal mucosa (Fig. 1). The parotid glands were neither swollen nor tender. She also developed a solitary urticarial lesion on the anterior chest wall but no bronchospasm, laryngeal, periorbital or lingual oedema and no cardiovascular disturbance. Treatment with intravenous chlorpheniramine 10 mg was given immediately, but neither adrenaline nor steroids were necessary. After 20 min the discomfort and the intense swelling reduced and gradually subsided over a period of several hours. By 24 h, the patient's facial appearance had largely returned to normal, but it was 2 weeks before she considered that the swelling had totally resolved.

The range of reactions to intravenous contrast media and their postulated mechanisms are well described by Ansell (1987). Angioneurotic oedema from various causes is reported to involve the eyelids in 69%, the lips in 65%, the tongue in 21% and other areas in 15% (Champion et al, 1969), Oedema confined to the cheeks and buccal mucosa is an unusual phenomenon, which does not appear to have been reported following use of intravenous contrast media.

Ansell (1987) states that the main value of H1 antihistamines is in the treatment of urticarial reactions of angioneurotic oedema, and in this case they proved satisfactory, without needing adrenaline or steroids.

The main differential diagnosis of this reaction is bilateral parotid gland swelling which is a well recognized, immediate, though transient reaction following use of contrast media which may last several hours (Navani et al, 1972; St Amour et al, 1986).

Angioneurotic oedema can present in a variety of ways and it is important that radiologists are aware of and can recognize the early signs of its development at unusual sites, so that prompt treatment may prevent more serious sequelae.

Yours, etc.,
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References

ANSELL, G. (Ed.), 1987. Contrast Media and Urography. In *Complications in Diagnostic Imaging* (2nd edn). Ed. by G. Ansell and R. A. Wilkins. (Blackwell Scientific Publications, Oxford), pp. 1–36.

CHAMPION, R. H., ROBERTS, S. O. B., CARPENTER, R. G. & ROGER, J. H., 1969. Urticaria and angio-oedema. A review of 554 patients. *British Journal of Dermatology, 81*, 588–597.

NAVANI, S., TAYLOR, C. E., KAUFMAN, S. A. & PARLE, R. H., 1972. Evanescent enlargement of salivary glands following tri-iodinated contrast media. *British Journal of Radiology, 45*, 19–20.

ST AMOUR, T. E., MCLENNAN, B. L. & GLAZER, H. S., 1986. Pancreatic mumps: a transient reaction to I.V. contrast media (Case report). *American Journal of Roentgenology, 147*, 188–189.

1990, *The British Journal of Radiology*, *63*, 232–234

Book reviews

Fundamentals of Radiology, 4th edn. By Lucy Squire and Robert A. Novelline, pp. xviii + 355, 1988 (Harvard University Press, Cambridge), £19.95.
ISBN 0–674–329626–0

This book is intended to be used as an aid for the interpretation of radiographs and other diagnostic images and is aimed directly at medical students.

It starts by introducing the reader to the basic concepts of X-ray production and then moves on the subject of radiographic interpretation. As with previous editions, much of the book is devoted to the chest and abdomen, dealing with these areas in some detail. Later chapters deal with the subjects of abdominal organ imaging, bones and neuroradiology. This 4th edition is well up to date. The use of ultrasound, scintigraphy, computed tomography (CT) and magnetic resonance has been addressed where appropriate. Reader participation is encouraged by the use of test cases scattered throughout the earlier chapters. This is a very user-friendly book, well laid out and easy to read. The fact that the authors repeatedly stress the need to interpret radiological findings in light of the clinical evidence and in consultation with radiological colleagues is good. Otherwise, it is without repetition.

There are a large number of illustrations which, with few exceptions, are of a very high standard. Colour diagrams have been used to demonstrate the pulmonary segments.

This book succeeds admirably in its objective. Not only medical students, but indeed many junior clinicians as well would benefit from this book. Although the book is to be recommended, its price seems excessive for individual purchase.

C. E. Williams

Paediatric Radiology. Self-Assessment in Radiology and Imaging. No. 6. By Christopher O'Callaghan, pp. 189, 1989 (Wolfe Medical Publications, London), £19.50.
ISBN 0–7234–0978–1

Although this book is part 6 of a series entitled "Self-Assessment in Radiology and Imaging" there is no indication who this "self" is meant to be and accordingly no standard by which to judge it. One hundred and fifty-one assorted paediatric imaging problems are depicted with accompanying potted history and questions on one page; the films are discussed and answers given on the reverse page.

The quality of the illustrations and the general production are good; the discussion very limited. The author has not caught up with ultrasound in the diagnosis of pyloric stenosis (just mentioned), intussusception, congenital dislocation of the hip. There is no list of contents at the front and the index at the back is extremely sketchy. There are no references. The book will therefore not answer questions or help with a problem and once read it is extremely unlikely to be looked at again. Who will want to read let alone buy it at the cost of an inexpensive meal for two? Perhaps a pre-examination student wishing to boost his moral, but even he would be much better off browsing through his hospital's X-ray museum.

G. M. Steiner

Contemporary Issues in Obstetrics and Gynecology: Obstetric Ultrasonography. Ed. by R. L. Berkowitz; and *Gynecologic Oncology.* Ed. by C. J. Cohen and N. G. Kase, pp. xiv + 246, 1988 (Churchill Livingstone, New York), £30.00.
ISBN 0–443–08601–X

This book tackles two separate subjects, the first being obstetric ultrasonography. This is not a comprehensive text, but a series of seven chapters, each covering a separate aspect of obstetric ultrasound. Each chapter discusses some basic findings and assumes very little background knowledge, but also goes into some detail of each subject, thus trying to satisfy the different requirements of the beginner and the expert.

As with all multiauthor texts the quality is rather varied, but the chapter on the placenta is particularly well written. However, the book is let down very badly by some poor illustrations, the majority of which are rather "elderly" B scans. Proof reading has also been rather lax in not noticing that figures 1–17 and 1–18 are identical, but with different captions.

Overall, this text is well produced and, apart from the illustrations, gives good reviews of the separate subjects. There is very little new in the book, but for those wishing to have a review of the more pertinent parts of obstetric ultrasound, this is a very useful text.

The second half of the book deals with gynaecological oncology. The seven chapters are devoted to a description of the possible pathogenesis of female genital tract malignancy. The chapters are short, generally well written and offer an excellent review, in the main, of most gynaecological cancers.

A few chapters tend to dwell on the personal reflections of the author. The sections represent the distillate of a symposium conducted at Mount Sinai School of Medicine in New York City. The exercise has been successful, although the reader is left with more questions than answers. It is worthy of perusal.

D. W. Pilling and R. G. Farquharson

Ultrasound of the Prostate. By B. D. Fornage, pp. xii + 333, 1988 (John Wiley & Sons, Chichester), £95.00.
ISBN 0–471–91257–3

In recent years transrectal ultrasonography (TRUS) of the prostate has come to be recognized as a valuable technique in the differential diagnosis of prostatic disease. The book reflects the author's experience over the past 10 years and traces TRUS from the original bistable equipment to the present-day hand-held multiplanar transrectal probes. It also covers the transabdominal and transperineal routes of prostatic ultrasound.

The first chapter deals with the anatomy of the prostate. The current thinking of the anatomy, as described by McNeal, bears no resemblance to the anatomy currently taught in medical school. The relevant anatomy is explained in a clear, concise way is the key to the understanding of endosonography of the prostate as the anatomy demonstrated by TRUS closely reflects and confirms the zonal anatomy recently described.

Although the author is a practising radiologist there is a considerable amount of clinical urology in the book, an understanding of which is important if we are to have a real impact on clinical management of prostatic disease. Chapters deal with the ultrasonic appearances of various benign conditions of the gland, a knowledge of which is necessary to allow differentiation from prostatic cancer.

The main emphasis of the book, quite correctly, is on the diagnosis, staging and assessment of the treatment response of prostatic cancer. However, there are further useful chapters on ultrasound guided biopsy, transrectal voiding cystourethrosonography and the possible artefacts and pitfalls of prostatic ultrasonography.

The book would be useful for any radiologist or urologist contemplating ultrasound of the prostate as it provides an excellent, balanced overview of the confusing and conflicting reports on this subject in the world literature. The emphasis, as in all ultrasonic examinations, is on the importance of technical considerations and the correlation between the sonographic appearances and pathology and histological considerations.

The text has a high editorial standard with good style, grammar and spelling and belies the fact that Dr Fornage's first language is French. The overall standard of the illustrations is very high but a minor criticism is that there are too many repetitive examples which fail to enhance the text.

I believe the author succeeds admirably in his aim of providing a comprehensive monograph on an important aspect of ultrasound. The book is rather expensive but still good value for such a beautifully bound book and should stand the rigours of multiple use by individuals and libraries.

G. J. GRIFFITHS

Imaging and Labelling Techniques in the Critically Ill. Ed. by W. Kox, J. Boultbee and R. Donaldson, pp. xvi + 188, 1988 (Springer-Verlag, London), £93.00.
ISBN 3-540-17483-4 (Berlin)
0-387-17483-4 (New York)

This book looks good, feels good and is good. It presents an up-to-date review of the role of modern imaging techniques in the management of critically ill patients. Clearly laid out and liberally illustrated with good quality images (apart from the inevitable poor quality portable chest radiographs in Chapter 5), the book packs an enormous amount of useful information into its 184 pages. Some may think the slim volume expensive at £93, but it fills an important gap in the literature.

The book is edited by an anaesthetist, a radiologist and a cardiologist, who are assisted by a team of contributors who are all recognized experts. They in turn represent the fields of anaesthetics, radiology, cardiology, nuclear physics, neurosurgery, physiology etc. There are five main sections devoted in turn to the neurological system, lungs, the cardiovascular system, the abdomen and special techniques. Each main section is then divided into chapters devoted to a particular imaging technique.

There are clear descriptions of equipment and apparatus (suitable for Part I FRCR and beyond). Interventional techniques are also included and there is a section on digital subtraction angiography. The text is well edited to produce a consistent style and layout. Each chapter is short and to the point and there is an abundance of useful practical advice. Most chapters refer to very recent work up to 1986 and even 1987 in some cases. There is even a reference to one of Starling's papers in the Journal of Physiology in 1886, so the book spans a century of intensive care!

There must be some criticism to prove that the reviewer has at least done his work thoroughly—Fig. 5.29 on page 62 is upside down.

This book is highly recommended; all those who are involved in the investigation and management of critically ill patients would benefit from reading its pages. It covers comprehensively subjects that are given only superficial treatment in standard radiological texts. The editors and publishers must be congratulated on a job well done.

G. M. ROBERTS

Emergency Radiology, 2nd edn. By T. E. Keats, pp. xiv + 515, 1989 (Year Book Medical Publishers, Chicago) £70.50
ISBN 0-8151-5044-X

This is a very ambitious book. The stated aim of the book is "To help the emergency physician get through the night", and it is about the radiology of acute trauma and disease. The book is split into chapters: the skull, the face, spine, chest, abdomen, pelvis and hips, extremeties and the paediatric patient. Each chapter includes sections on radiographic technique and anatomy, pathology and normal variants. Information on the use of computed tomography, ultrasound and arteriography is included where indicated.

As is common in books with multiple authors, some chapters are better than others. I particularly liked the chapter on the chest which I think is suitably balanced and gives a fair appraisal of the subject. The abdomen is a more difficult topic and not all centres would agree on the modes of investigation. For instance not everyone would agree on the need for erect and supine abdominal films in the acute abdomen, nor the need for upright films to be obtained on debilitated patients with the help of compression binders. With respect to the spleen there are different views about the investigation of this area and I think a more balanced view would have been useful. As stated in the introduction to the chapter, the view expounded by the authors is a simplification of material present in the literature. Two other points: first, rupture of the diaphragm is inadequately covered and secondly, the ten day rule is no longer in operation in this country.

The section on the skull is good. The one on the face is marred only by the vast amount of material on fractures of the mandible. The chapter on the spine leaves much to be desired and I do not think this chapter in any way addresses the problem of helping the physician to diagnose or exclude spinal injury competently. There is no attempt to guide the physician through the examination of the spine. This is an area of the body which lends itself to systematic analysis and this should be the basis of interpretation. Fracture/dislocations and fractures of the odontoid peg are markedly undercovered.

The chapter on the pelvis and hip is good; the one on the extremities is extremely poor. The latter can partially be explained by the fact that this is not a book about fractures. It is noticeable that fractures which cause other acute complications, for example, dislocations of the foot and ankle that are likely to cause skin damage, and fractures around the knee causing vascular impairment are not well documented. There is much in this chapter with which I disagree. There are factual errors, for example, the statement that arthrography demonstrates ligamentous tears for only approximately 24 hours is untrue.

The paediatric chapter is short but its scope is suitable. Unfortunately, the radiographs have not reproduced well. Some of the text is difficult to understand and it would have been helpful if the radiographs had been well annotated.

As one would expect, the sections on normal variants are good and the pictures are excellent. In the book as a whole there are only occasional minor errors in spelling and indexing.

This book is an attempt to put together in a single volume a large amount of material. Many of its shortcomings are due to this compression, but some parts of the book in my opinion are misleading. I think that the emergency physician would be better advised to consult individual texts available about the individual topics in this book. I would not recommend this book for the individual buyer, but some of the chapters are definitely worth reading.

DAVID FINLAY

Congenital Heart Disease. A Diagrammatic Atlas. By C. E. Mullins and D. C. Mayer, pp. xlii + 352, 1988 (Alan R. Liss, New York), $72.50.
ISBN 0-8451-4255-0

The adage that a picture is worth a thousand words was never more appropriate than in the description of congenital heart defects. The authors offer 167 line diagrams illustrating the common congenital cardiac defects including all the more difficult-to-draw variations in atrio-ventricular and ventriculo-arterial connections, cardiac positions, atrial situs and aortic arch lateralization. The common operations are also illustrated. The diagrams are simple, two dimensional and not "arty". The book is spiral bound to make photocopying easy. The nomenclature is always a thorny issue in the description of complex congenital heart disease; the diagrams are discretely labelled and the authors have steered tactfully between the various schools of the nomenclature.

Showing the book around the unit, it was admired by nurses teaching their juniors, by junior doctors struggling with the seemingly infinite variety of congenital heart disease and all those communicating with parents.

People "in the business" would not buy the book for their own benefit but it will be a great asset to teaching libraries and towards dealing with children with heart defects. There it will be a godsend, helping through the usual initial apology of "my drawing is not very good but it is something like this".

An off-beat book for which the authors deserve congratulations and thanks.

C. Bull

Pocket Atlas of Cardiac and Thoracic MRI. By Jeffrey J. Brown and Charles B. Higgins, pp. viii + 63, 1989 (Raven Press, New York), $17.00.
ISBN 0-88167-488-5

This inexpensive, pocket-sized paperback is part of a series published by Raven Press on MR anatomy. The first section of the book covers the anatomy of the thorax with spin-echo images in transaxial section, a few sagittal and coronal sections and sagittal oblique images through the aortic arch. The majority of these were obtained at 0.35 Tesla, but there are a few transaxial images at 1.5 Tesla and eight gradient-echo images showing the enhancement of signal seen with flowing blood using this sequence. The illustrations are well reproduced and the anatomy clearly marked, although in the transaxial plane, the anatomy of the mediastinum is very basic for those with any CT experience.

The second section demonstrates a number of congenital vascular anomalies with some examples of thoracic pathology including an aortic dissection and tumours in and around the heart. One or two of these are superfluous, particularly one showing a malignant giant cell tumour of bone metastatic to the left atrium.

This book is good value for money and continues this series of convenient reference books on MR. It should appeal to radiologists and radiographers starting in magnetic resonance and will no doubt find a place among the reference books found in the control rooms of scanning units. It is not likely to be very useful for those who are already familiar with anatomy of the heart and great vessels who will require a more detailed textbook of anatomy and pathology.

J. B. Bingham

Pocket Atlas of Head and Neck MRI Anatomy. By Robert B. Lufkin and William N. Hanafee, pp. viii + 76, 1989 (Raven Press, New York), $17.50.
ISBN 0-88167-498-2

This 76-page book is the latest in a series of pocket MRI atlases from the Raven Press. It is presented by two widely respected authors in the field. It covers the normal anatomy of the neck, para-nasal sinuses, pharynx and skull base including a section on the temporal bone. The intracranial and intraspinal contents are not included in this book but are presented in another of Raven Press's pocket atlases. Sagittal, axial and coronal images are shown.

The illustrations are high quality T_1-weighted images printed on glossy paper, with an accompanying pilot view in another image plane, an idea used to good effect on every page. The images are clearly labelled in almost all cases except one or two examples, for instance in the section on the temporal bone, where the structures to which the arrows point cannot be seen. However, this is a very useful book and maintains the high standard set by the previous atlases in the same series.

It will be useful to radiologists, clinicians and all those wishing to learn multiplanar anatomy. Those who will most appreciate it are, I feel, radiologists and radiographers who are just getting to grips with the complexities of MRI. It is truly a pocket-sized book and good value at $17.50.

P. McCarthy

BIR Bulletin

Honorary Editor, BIR Bulletin: D. Rickards, LRCP, MRCS, FFR(D)SA, FRCR
Please address all correspondence to: Honorary Editor, BIR Bulletin, The British Institute of Radiology, 36 Portland Place, London W1N 4AT

The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

Change at the helm of the BIR

In September 1989, after Susan Johnstone had completed more than five years as General Secretary of BIR, she decided that she would enjoy taking a break from being in the hot seat and asked to resign at the end of the year. In fact, Susan has helped to steer the Institute through a very choppy stretch of its course. Five years ago, for example, we were still in deep trouble following the move to Portland Place from Welbeck Street, but now, although conditions are still pretty lively, the whole ship has a much more secure feel to it. Dropping a good pilot is always an occasion for anxiety, even if this is offset by a feeling that many of the worst rocks may be behind you.

In January Susan is setting off for points east: first stop Thailand, then Malaysia and to Nepal in March, with thoughts of getting to Greece in early summer before the rest of us crowd it out. We shall miss her enormously, and doubtless have many an occasion to think that she has taken the wise course.

Susan's successor is Mary-Anne Piggott who is taking over from 1 January, following a couple of weeks' overlap. Mary-Anne has a background in research and business, together with a three-year stint on the staff of the Royal College of General Practitioners, some of whom she says she found "very sparky"! We hope we can match that, and look forward to having her on board.

C. R. Hill
BIR President

Outgoing General Secretary Susan Johnstone with most of the people who make the BIR go.
Seated, from left to right: Dolly Douglas, Receptionist/Membership; Gunnel Ingham, Librarian; S. J.; Katy Fletcher, Assistant Editor, BJR.
Standing, from left to right: Tony Hudson, Administration Manager, Nelleke van Helfteren, Conference Manager, Charlotte Mcleish, Administration/Calendar Assistant; Helen Smith, Advertising Co-ordinator; Tim Hogan, Publications Manager; Jackie Brunner, Publications Secretary; Claire Brice, General Secretary's PA; Terry Moran, House Manager.

The British Radiological Library has arrived

Plans laid several years ago have now borne fruit with the introduction, at 36 Portland Place, of an enhanced library scheme as a joint venture between the BIR and kindred organizations. This has been made possible by two developments: first, the joining of the scheme (initially on a three-year trial basis from January 1990) by The College of Radiographers and British Medical Ultrasound Society and secondly, a magnificent donation, totalling £75000 over a period of five years, from British Nuclear Fuels plc.

The increased resources that these two developments together provide should make radical improvements possible in both the current and the archival collections of the former BIR library, and also in the general level of library service that can be provided to members of the existing and future participating societies. Detailed plans are still being drawn up, and the Librarian and Library Committee would welcome members' views on what they would like to see. Almost certainly, however, we shall use the opportunity to introduce appropriate information technology, with access to bibliographic databases such as Medline and, in extending our collections, we will aim to provide a broadly based source for educational reading and reference whilst choosing judiciously to build up more specialist research and archival collections, in particular areas that seem not to be well served elsewhere in the country.

There will undoubtedly be problems, and not least one experienced by all libraries, that of housing an increasing collection of material in limited space. However, if carefully and imaginatively managed, the new scheme should be able to provide the broad-church UK radiological community with a major and valuable intellectual resource. It will be up to individual members to make good use of it and help to guide it in the right direction. We look forward to seeing and hearing from you!

C. R. Hill
BIR President

Curt Westman Scholarship

Members wishing to visit the clinic in Vallingby, Sweden, of the late Dr Curt Westman, now owned by AB Medicinsk Rontgen, should write to the General Secretary of the BIR. Return air fares and 2 weeks' accommodation are generously provided by AB Medicinsk Rontgen, and the BIR provides a sum towards expenses.

Library News

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays).

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–7 p.m. and Thursdays 11 a.m.–5p.m. In her absence, assistance will be given by Miss Helen Smith. (Tel: 01-580 4085.)

The journal stock includes more than 100 titles. Though journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

Recent additions to the Library

Bo, W. J., Wolfman, N. T., Krueger, W. A. & Meschan, I.,1990. Basic atlas of sectional anatomy with correlated imaging, 2nd edn.

Hüpscher, D. N.,1988. Radiology of the oesophagus.

ICRU, 1987. Report 42: Use of computers in external beam radiotherapy procedures with high-energy photons and electrons.

ICRU, 1988. Report 43: Determination of dose equivalents from external radiation sources. Part 2.

Langland, O. E., Langlais, R. P., McDavid, W. D. & DelBaso, A. M., 1989. Panoramic radiology. 2nd edn.

Middleton, W. D. & Lawson, T. L. (Eds), 1988. Anatomy and MRI of the joints — a multiplanar atlas.

Reed, K. L., Anderson, C. F. & Shenker, L., 1988. Fetal echocardiography. An atlas.

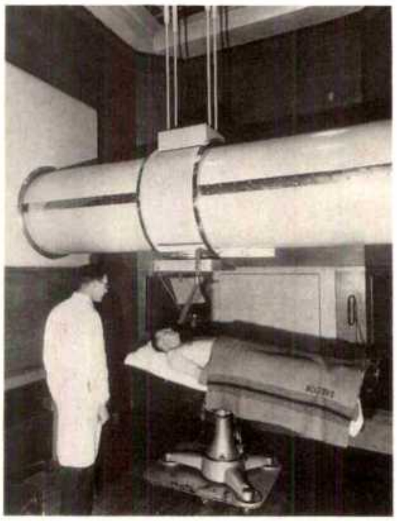
Notice from the librarian

ICR: Paris 1989

If any member has literature to spare from last Summer's ICR Conference, the librarian would be very grateful for a donation.

Obituary
Ralph Phillips, MS, FRCS, FFR, DMRE

Dr Ralph Phillips, whose name will always be associated on both sides of the Atlantic with the development of megavoltage radiotherapy, died in the United States on 17 July 1989 at the age of 86. He died at his home in the green hills of Mendham, New Jersey, so like those of his native England from which he had emigrated over 40 years before. In this country he is remembered particularly for the development and investigation of million-volt X-ray therapy at St Bartholomew's Hospital in London in the period 1937-1945, and this photograph shows him using the equipment at that time.



Born in London, he was at school at Christ's Hospital at Horsham, and from his early boyhood he was set on a career in surgery. At the Medical College of St Bartholomew's Hospital his career was one of particular distinction, for he achieved not only the Senior Scholarship (in medical sciences) but then the Brackenbury Scholarship in Surgery and later, as a postgraduate, the Luther Holden Research Scholarship in Surgery. He qualified in 1927 and went on to attain the MS (Lond.) and the FRCS (Eng.), and having held surgical posts and the Senior Demonstratorship in Anatomy was set fair for a distinguished career in his chosen subject. But increasing experience and interest in neoplastic disease led to a change of direction. Joining N. S. Finzi as Chief Assistant in the Radiotherapy Department at Bart's, and having obtained the DMRE (Camb.) in 1933, he applied himself with remarkable devotion to the development of radiotherapy. For more than a decade the influence of his sterling character and outstanding ability had a remarkable effect in moulding attitudes to the newly developing specialty within his own teaching hospital: scientists and clinicians alike respected his intellectual qualities and impeccable surgical antecedents.

No-one had undertaken the development of X-ray therapy with greater vigour than N. S. Finzi, who since 1912 had directed the X-ray department at Bart's and had, from his experience of step-wise progressions, become convinced of the advantages of higher and higher energies. Moreover Finzi, who was a pioneer of radium therapy, foresaw advantages additional to those of increased penetration if the gamma rays of radium could be simulated by X-radiation of comparable energy. This, of course, implied attaining one million volts. The way in which this was achieved by T. E. Allibone at Metropolitan Vickers, and the equipment designed and installed in 1936 at St Bartholomew's Hospital, were recently described at a conference to mark the 50th anniversary of megavoltage radiotherapy (*Supplement 22, British Journal of Radiology*, 1988). Ralph Phillips was ideally suited to undertake this exciting research and was duly appointed to a Halley Stewart Fellowship. While the conception of the million volt project was due to Finzi, Hopwood and Canti, its maturation and success were undoubtedly due to the close collaboration between Ralph Phillips and George Innes, the engineer and physicist. By 1937, following very detailed physical investigations, treatment was started at 700 kV, and from 1939 continued at the planned 1000 kV. The skin erythema dose was 50% higher than at 200 kV, and detailed isodosimetry on each individual patient helped define tolerance doses in respect of connective tissue and critical organs. As to tumour response, as early as 1938 Phillips was able to demonstrate complete regression of inoperable rectal carcinoma (and this patient was to survive for over 20 years). No sooner was the investigation proceeding smoothly and attracting a great deal of attention than the clouds of the Second World War broke, and as Bart's, in the City of London, was in a very vulnerable position, many of its facilities had to be dispersed. Ralph Phillips remained as the sole radiotherapist, running both the deep X-ray and the supervoltage departments. Throughout the Blitz the million-volt equipment continued to function with minimal interruption of treatments, despite transient loss of protective doors, windows and even the moving floor from concussion and bomb fragments. It was a privilege to have seen Ralph Phillips and George Innes coping with both the clinical load and the research investigation throughout this period. Not surprisingly, Phillips become ill, and the fact that he completed the investigation under the trying circumstances of the war and of his own ill health was a tribute to his courage and tenacity. By this work were established the now well-known advantages of a beam of megavoltage energy: in comfort to the patient (by reduced skin reaction and integral dose), optimized planning and widening the scope of radiation therapy. *Supervoltage X-ray Therapy*, a joint effort by Phillips and Innes, was published in 1944 and recognized on both sides of the Atlantic as a landmark in the development of radiotherapy.

Just before embarking on the million-volt project, Ralph Phillips had met the distinguished American James Ewing (of "Ewing's tumour") at the Brussels Cancer Congress of 1935 and had escorted him on his subsequent visit to London. Ten years later, and following the publication of *Supervoltage X-ray Therapy*, Ewing recalled the clear-minded yet modest young Englishman, and determined to secure him for the Memorial Hospital in New York. Thus on the crest of his investigational wave, and attracted by the prospect of developing facilities, he migrated to the United States to start what he termed his "second career". Just six weeks after starting work in New York he suffered a serious recurrence of his chest illness and his life became in jeopardy. Fortunately streptomycin had become available there; he was included in the trial and responded dramatically. In a letter to the Lancet in 1947 he graphically described his clinical picture and the response to treatment, and urged those responsible for decision making in the UK to get on with the production of streptomycin in adequate quantities, on the evidence then available. Despite his multiple disabilities he was able to resume a productive career and to commute daily from Mendham, New Jersey across the Hudson River to Manhattan for the next twenty years.

As Attending Radiation Therapist at the Memorial Hospital he continued the clinical investigation of megavoltage therapy and extended his interest in bone tumours and childhood cancer, and in both fields made important contributions. In 1952 he was Hunterian Professor of the Royal College of Surgeons; from the same year Professor of Radiation Therapy at Cornell University; and he later became Departmental Chairman at Memorial–Sloan Kettering. He had the devoted confidence of his clinical colleagues, and generations of interns and residents were grateful for the inspiration and guidance of this kindly man who was the epitome of English manners. His retirement from Memorial-Sloan Kettering in 1968 was marked by a notable international symposium in his honour. For several years afterwards he gave his services to community hospital radiotherapy in New Jersey and kept up his lively interest in the subject.

Ralph Phillips was an inspiring figure, a skilled and compassionate clinician who made major and enduring contributions to the development of radiotherapy. A remarkable man, of outstanding intellect, yet always charitable, his innate modesty remained with him throughout his life. When the "50th Anniversary of Megavoltage Radiotherapy" conference was held at Bart's in 1987 he was, at the age of 85, unfortunately unable to be present, but nevertheless took the keenest interest in the proceedings. The courage and tenacity with which he overcame so many difficulties were for decades a source of admiration to his friends on both sides of the Atlantic. He is survived by his wife, Barbara, and by his son, Paul who is Professor of Medicine at Syracuse, New York.

ARTHUR JONES

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

Impact of modern imaging techniques in everyday ENT practice
January 18, 1990
Joint BIR/RCR/RSM evening meeting organized by the BIR
Chairman: Dr P. Anslow

Methods of determining blood flow using radionuclides
February 13, 1990
Joint IPSM/BIR all day meeting organized by IPSM

Quantitation of argon blood flow using nuclear medicine techniques
February 21, 1990
Chairmen: Drs R. Speller and W. Hately

Radiobiology proffered papers
February 23, 1990
All day work-in-progress meeting

Imaging towards 2000 — practical integration of new technologies
March 21, 1990
All day meeting at the Scientific Societies, London
Chairmen: Profs P. N. T. Wells and I. Isherwood
Speakers: R. Frakowiak, A. Hemingway, J. Howart, W. R. Lees, H. Nunnerly, M. Smith and J. Williams

Conversazione
March 21, 1990
Royal College of Physicians, Regent's Park, London.
Lecture by Ms Olivia Wilson on veterinary radiography.

Photodynamic therapy
April 4, 1990
Joint BIR/IPSM all day meeting organized by the BIR
Chairman: Dr D. Ash

BIR Annual General Meeting
May 3, 1990 at 5 p.m.
36 Portland Place, London
BIR members only

The combination of chemotherapy and radiotherapy in clinical practice
May 10, 1990
All day meeting
Chairmen: Prof. A. Horwich, Dr J. Tobias and Dr S. Arnott

The repair of radiation damage — molecules to man
May 11, 1990
All day work-in-progress meeting

Radiology 90
Harrogate, 11-13 June 1990

Deadline for receipt of proffered abstracts for work in progress is 15 April 1990. Please contact the Conference Office for an abstract form.

Annual Report of the Executive Committee of the Hong Kong Branch of the BIR (1988–1989)

This year sees a record of 191 paid-up members (including UK membership) with 70 radiologists and 121 radiographers. The members come from a range of government, subvented and private hosptals.

Three meetings were held this year. The inaugurating lecture was given by M. T. Chau: "Ultrasound features of recurrent pyogenic cholangitis and hepatocellular carcinoma" on 8 July 1988, when the Annual General Meeting was also held.

The second lecture was held on 22 August 1988 in the Hong Kong Sheraton Hotel: "Chemotoxicity of iodinated contrast media and update on current issues", given by P. Dawson.

The third lecture was given on 1 May 1989 by the world-renowned Harold G. Coons: "Artery angioplasty and percutaneous gastroscopy".

All these meetings were encouragingly well attended.

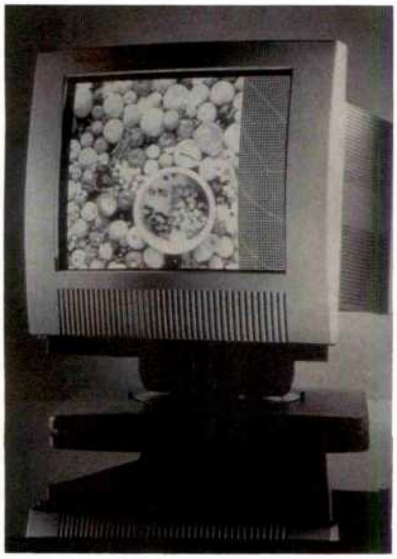
I am also happy to announce that the financial situation this year is healthy and sound.

At the AGM, the following members were elected as follows: W. Ngai Wan as Chairman, Lau Kam-Ying as Honorary Treasurer and R. Leung Wai-Man as Honorary Secretary.

WINNIE NGAI
CHAIRMAN

Product news

X-ray film quality from Megascan



CGI Computer General Ltd have recently introduced the Megascan Medical Display System (MDS) which provides 2560 x 2048 x 12 grey scale image resolution at 200 dots per inch (dpi), the highest grey scale resolution available. The flicker-free display achieves the resolution generally regarded as necessary for diagnosis from digitized X-rays. Megascan's multiple windowing facility allows separate images to be displayed together on screen with each being adjusted for optimum viewing.

MDS is compatible with PCs, Sun work stations and other VME based systems.

Pricing ranges from £5000 to £20000, depending on configuration.

For further information contact Dick Selwood, Winterbourne Communications. Tel: 0962 840830.

Blood flow analysis system

Oxford Sonicaid has developed a comprehensive bi-directional Doppler system with integral spectrum analyser of peripheral vascular examinations and utero-placental studies: the VASOFLO 4. One of many features is the ability to enter a probe-vessel angle; the display scale and the automatically calculated waveform parameters are then shown in cm/s.

Rapid patient examinations can be obtained through improved Doppler sensitivity, diagnostic waveform interpretation in real time and high speed printing of results. The large 14" colour monitor aids visual interpretation of the Doppler spectrum and gives a clear indication of operating mode. Examination results can be printed via the optional integral thermal printer. Colour hard copies of any screen display may also be produced at low cost using an external colour ink-jet printer. The printer buffer can store, on average, ten displays.

For further information contact: Oxford Sonicaid Ltd, Quarry Lane, Chichester, West Sussex PO19 2LP. Tel: 0243 775022.

New Nordian blood product irradiator

Nordian International has introduced a new blood product irradiator, the Gammacell 1000 Elite. Features of this latest model include a battery supported DC drive and control system, an industrial quality tactile key pad, two-line alpha numeric display of user entered irradiation parameters and a computer-compatible output for this data.

Nordian International are the successors to Atomic Energy of Canada Ltd Radiochemical Company and are represented in the UK by Vinten Analytical Systems Ltd, Sunderland Road, Sandy, Bedfordshire SG19 1RB. Tel: 0767 82222.

BIR Company Subscribers

The BIR company subscriber scheme was launched at the end of 1987 and is aimed at all companies who advertise in the BJR or exhibit at the MED X RAY technical exhibition.

For a subscription of just £250 per annum for an initial period of 3 years, an attractive package of benefits is offered (see March 1988 Bulletin for details).

If your company is interested in joining the scheme, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 01-580 4085. Companies that have enrolled to date are listed below.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex TW8 9AX; tel. 01-560 2131. Product Areas 1. Contact Mr G. Mountford, Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury, Bucks HP20 2TP; tel. 0296-395222. Product areas 4, 5, 6. Contact Mr James McLaughlin, Sales and Marketing Manager.

British Nuclear Fuels plc
Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS; tel. 0925-835022. Product areas 8, 11. Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Cardiac Services Ltd
95A Finaghy Road, South Belfast BT10 OBY; tel. 0232-625566. Product areas 1, 3, 4, 5, 6. Contact Mr R J Brown, Managing Director.

Central Electricity Generating Board
15 Newgate Street, London EC1A 7AU; tel. 01-634 6898. Product areas 7, 8. Contact Mr R. V. Brierley, Office Services Manager.

E. G. & G. Astrophysics Research Ltd
Vale Road, Windsor, Berkshire SL4 5JP; tel 0753-855611. Product areas 1, 6, 7, 8,. Contact Miss Susan Holgate, Sales Executive (Therapy).

Elscint (GB) Ltd
Tower Road, Berinsfield, Oxfordshire OX9 8LW; tel 0865-340900 . Product areas 1, 3, 4. Contact Ms Faith Gorman, Managing Director.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20; tel 01-446 9714. Product areas 1, 2, 8. Contact Mr D. F. Wills, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London NW3 6JH; tel 01-586 9351. Product areas 1, 3. Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
4 Clarendon Chambers, Clarendon Street, Nottingham NG1 5LN; tel. 0602-483807. Product areas 1, 3, 4, 5, 6. Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks SL1 4ER; tel. 0753-874000. Product areas 1, 3, 4, 5, 6, 8. Contact Mr Jack Strange, Sales Administration.

Kodak Ltd
PO Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU; tel. 0442-61122. Product areas 1. Contact Mr P. E. Blackwell, Manager, Health Sciences Division.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ. tel. 0604-46132. Product areas 4, 5. Contact Mr D. G. L. Wood, Business Manager.

Medical XraySupplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU; tel. 01-205 9500. Product areas 1. Contact Mr R. J. Laird, Sales Director/Managing Director.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA; tel 516-741 7614. Product areas 1, 3, 4, 5, 6, 8. Contact Mr H. Glasser, General Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA; tel 021-742 2444. Product areas 1, 3. Contact Mr L. Birch Hansen, Managing Director.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ; tel: 01-741 1666. Product areas 1, 3–8. Contact J. M. Woolston, Sales and Marketing Manager.

Polaroid (UK) Ltd
Ashley Road, St Albans, Herts AL1 5PR; tel: 0727 59191. Product areas 1, 3. Contact Ms Tina Thompstone, Product Supervisor.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR; tel. 09277-67433/63320. Product areas 8. Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA; tel: 0635-32222. Product areas 2, 10. Contact Mr Christopher Trim, Publicity Officer.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE; tel: 04446-6011. Product areas 1, 2, 3. Contact Mr A. Greaves, Product Manager.

3M UK PLC
3M House, Bracknell, PO Box 1, Berks RG12 1JU; tel. 0344 426726. Product areas 1. Contact Mr Alan Budge, Marketing Manager.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands; tel. 015 61 0121. Product areas 1, 6. Contact Mr. P Blonk, Office Manager, X-ray BU.

Wardray Products Ltd
Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP; 01-398 9911. Product areas 8. Contact Mr R. B. Wardley, Managing Director.

Key to product areas:

1. Diagnostic X-ray inc. NMR and CT.
2. Interventional radiology.
3. Ultrasound.
4. Nuclear medicine.
5. Radiopharmaceuticals.
6. Radiotherapy and oncology.
7. Radiobiology.
8. Radiation protection.
9. PACS.
10. Image processing.
11. Nuclear fuel cycle services.

Meetings and Courses

Magnetic Resonance for Diagnosis
18 January, 1990
London
Further details: The Scientific Meetings Officer, The Royal College of Pathologists, 2 Carlton House Terrace, London SW1Y 5AF. Tel: 01-930 5861.

Current Status and Future Directions of Immunoconjugates Monclonal Antibody-based Imaging and Treatment II
February 15–17, 1990
Orlando, USA
Further details: Division of Continuing Medical Education (D23-3), University of Miami School of Medicine, PO Box 016960, Miami, Florida 33101, USA. Tel: 305 547 6716.

Clinical Oncology Symposium: Radiotherapy as an Adjuvant Treatment in the 90s: a Critical Review
February 16, 1990
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG. Tel: 01-636 4432.

Eighth Winter Congress, Diagnostic Imaging
March 10–17, 1990
Switzerland
Further details: Winter Congress, Medical Seminars International, 9800 D Topanga Canyon Boulevard, Suite 232, Chatsworth, California 91311, USA.

33rd Annual Diagnostic Radiology, Postgraduate Course
March 19–23, 1990
San Francisco, USA
Further details: Radiology Postgraduate Education, University of California, 521 Parnassus Avenue, Room C-324, San Francisco, CA 94143, USA. Tel: (415) 476 5731.

Theoretical Course on Obstetric Ultrasound
March 26–30, 1990
London
Further details: The Postgraduate Education Office, The Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent's Park, London NW1 4RG. Tel: 01-262 5425.

Diagnosis and Treatment of Neoplastic Disorders: Medical, Surgical and Radiotherapeutic Aspects
March 29–30, 1990
Maryland, USA
Further details: Program Coordinator, The Johns Hopkins Medical Institutions, Office of Continuing Education, Turner Building, 720 Rutland Avenue, Baltimore, Maryland 21205, USA.

Advanced Imaging of the Muscoskeletal System
April 14–15, 1990
California, USA
Further details: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: 404 641-9773.

2nd International Brachytherapy and Remote Afterloading Symposium and Workshop
April 19–21, 1990
St Louis, Missouri
Further details: Carlos A. Perez, Director, Radiation Oncology Centre, Mallinckrodt Institute of Radiology, 4511 Forest Park Boulevard, Suite 411, St Louis, Missouri 63108, USA.

Advances in Ultrasound: East Anglian Ultrasound Group Ultrasound Study Day
April 21, 1990
Peterborough
Further details: Dr R. E. Moshy, Consultant Radiologist, Peterborough District Hospital, Thorpe Road, Peterborough PE3 6DA. Tel: 0773 67451, Ext. 4426.

Euroson 90
7th Congress of the European Federation of Societies for Ultrasound in Medicine and Biology
May 6–11, 1990
Jerusalem, Israel
Further details: The Secretariat, PO Box 50006, Tel-Aviv 61500, Israel. Tel: 03 654571. Extended abstract deadline: January 31, 1990.

Magnetic Resonance Imaging and Spectroscopy (Spring Course)
May 28–June 1, 1990
Norway
Further details: MR-Center, The Educational Program, N7034 Trondheim, Norway. Tel: 47 7 597700.

Muscoskeletal Imaging
July 23–25
California, USA
Further details: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: 404 641-9773.

The Fourth Annual Symposium on Magnetic Resonance Imaging
July 26–29, 1990
California, USA
Further details: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: 404 641-9773.

4th Annual Meeting of the European Society of Head and Neck Radiology
September 12–15, 1990
Brescia, Italy
Further details: The Organizing Secretariat, Clas International S. r. l., Via Pace, 8, 25122 Brescia, Italy. Tel: 9 30 48006.

Third Annual Applied Ultrasound: Accent on Doppler
September 12–15
California, USA
Further details: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: 404 641-9773.

Edinburgh 90: The Royal College of Radiologist's Annual Scientific Meeting and Exhibition
September 18–21, 1990
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London W1N 3DG. Tel: 01-636 4432. Abstract deadline: April 20, 1990.

First International Congress on Very Ultra Low Dosage
September 20–22, 1990
Bordeaux, France
Further details: VULD, Secretariat, Hematology Laboratory, Faculty of Pharmacy, 3 Place de la Victoire, 33076 Bordeaux, France. Tel: 3356913424 Ext. 711. For inquiries about abstracts: Professor Ch. Doutremepuich. Deadline for abstracts: March 1, 1990.

23rd Annual Meeting of the European Society for Radiation Biology
September 23–26, 1990
Dublin, Ireland
Further details: Dr C. B. Seymour, Radiobiology Research Group of the Nuclear Energy Board, Geological Survey of Ireland, Beggars Bush, Dublin 4, Ireland. Tel: 01 609511, Ext. 420.

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR Bulletin.

Radiology 90

Harrogate, 11-13 June 1990

Harrogate

Centrally situated at the heart of North Yorkshire, Harrogate is a charming town that started as a centre for visitors and that has since adapted its amenities to cater for the demands of its mod-ern day international clientele.

Surrounded by the rolling moors and dales, pretty villages and places of interest, Harrogate provides the perfect opportunity to sample the elegance, architecture and standard of service befitting a resort that has attracted the attentions of the public for over 400 years.

After the discovery of the spa waters in Harrogate, the aristocracy flooded to the town to "take the waters" both externally and internally and this popularity gave rise to the rapid development of first-class shops amidst broad, tree-lined streets, parks and gardens, excellent hotels, majestic public buildings, theatres and restaurants.

Harrogate is "England's Floral Town" having repeatedly won the Britain in Bloom competition, and throughout the streets visitors will find a living carpet of colour. Monpellier Gardens, Crescent Gardens and Prospect Gardens reflect ever changing floral backdrops, while the world famous Valley Gardens progress from formal flower beds to rose gardens, rhododendrons and sweet-smelling acres of pine forests.

Modern Harrogate is a prosperous and thriving tourist and conference/exhibition venue, annually entertaining hundreds of thousands of visitors on both business and pleasure, or even combining the two! Portraying the spa heritage, the recently restored and refurbished Royal Pump Room Museum houses the original sulphur well amidst various visual displays of early Harrogate.

Within easy reach of Harrogate there are literally hundreds of places of interest including Knaresborough, a picture-book market town; the historic cathedral city of Ripon; Fountains Abbey: awe inspiring ruins of a Cistercian Monastery; Brimham Rocks: weird and wonderful rock formations; Newby Hall: eighteenth century stately home; Ripley Castle: home of the Ingilby family for over 600 years; Lightwater Valley Leisure Park and Old Mother Shipton's Cave and Petrifying Well.

Your Chance to Learn about CT Imaging in the Head and Neck

Dr J. E. Gillespie and Dr A. Gholkar co-present a teach-in at Radiology 90 in Harrogate

Wednesday June 13, 2.30–3.45 p.m.

The evaluation using computed tomography (CT) of non-CNS abnormalities of the head and neck represents a challenge to most radiologists. Careful planning is needed beforehand, as there are a variety of ways to scan this anatomically complex area. Decisions regarding slice thickness, desired image planes (direct multiplane scanning or multiplanar reformatting, either 2D or 3D), the need for intravenous contrast media and dynamic data acquisition, and radiation dose factors all need to be made prior to the examination and tailored to both the patient's clinical condition and the clinical question to be answered.

The session will focus upon the CT approach to neoplastic and traumatic abnormalities of the extracranial head and neck. Relevant anatomy will be presented along with pathological appearances as well as the pros and cons of different CT techniques. The increasing role of MRI, particularly in relation to neoplasia, will also be discussed.

Adequate time will be provided in the final part of the "teach-in" for what we hope will be an open discussion on the topics presented.

BIR Bulletin

Honorary Editor, BIR Bulletin: D. Rickards, LRCP, MRCS, FFR(D)SA, FRCR
Please address all correspondence to: Honorary Editor, BIR Bulletin, The British Institute of Radiology,
36 Portland Place, London W1N 4AT
The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

28TH CONVERSAZIONE

Royal College of Physicians, Regent's Park

Wednesday 21 March 1990, 6.30 p.m.

The Conversazione is the Institute's informal gathering, not just of members but also of family and friends. It is a relaxed and sociable time, an opportunity for meeting old friends and making new ones.

The evening will start with a reception in the elegant library, following which the BIR awards will be presented by the President who will also welcome the new Honorary Members of the BIR.

The guest speaker this year will be the radiographer Mrs Olivia Wilson, whose talk will be "Aardvarks, apes and alligators — ultrasound and X-ray at London Zoo". This lecture, based on her work with animals of all types during five years spent at the Institute of Zoology, Regent's Park, will doubtless entertain and inform all the members of the audience. A fork buffet with wine will be served after the lecture.

Please contact the BIR Conference Office for a programme and registration form.

Radiology 90

Harrogate, 11-13 June 1990

Radiotherapy for soft tissue sarcomas: a challenge

Review Lecture

Dr C. L. Harmer

Wednesday 13 June (afternoon)

The problem of local recurrence of soft tissue sarcomas remains a challenge. Even with optimal surgical treatment comprising wide resection, local recurrence will follow in from 40% to 60% of patients unless radiotherapy is also given. Radiotherapy is usually required except for low grade tumours where a good margin of clearance has been achieved on the deep aspect as well as elsewhere.

The Soft Tissue Sarcoma Unit of the Royal Marsden Hospital was established in 1973 and ensures that all patients are seen in combined consultation with the surgeon so that optimal management can be planned. Amputation can usually be avoided by a limb-conserving procedure supplemented with high dose irradiation. A good functional and cosmetic result can thereby be achieved.

Pharmacological stress provides a more sensitive test for the diagnosis and management of coronary artery disease than dynamic exercise.

Dr Richard Underwood, the Senior Lecturer in Cardiology at the National Heart and Lung Institute, will present a review of his and his colleagues' work at Radiology 90 on Tuesday 12 June (morning).

Pharmacological stress in the diagnosis and management of coronary artery disease

S. R. Underwood, D. J. Pennell, R. S. O. Rees and D. B. Longmore

Magnetic resonance (MR) imaging provides detailed anatomical and functional information about the cardiovascular system, but its application in patients with coronary artery disease, the disease that kills a third of the population of the Western world, has been hampered by the difficulty of imaging during dynamic exercise. Pharmacological stress is a promising alternative and workers at the National Heart and Lung Institute have investigated the potential of intravenous dipyridamole and dobutamine. The former has been successfully used in thallium 201 myocardial perfusion imaging, and a comparison of thallium 201 emission tomograms with cine MR images acquired after dipyridamole infusion has shown that only 60% of thallium defects correspond with myocardial ischaemia and hence wall motion abnormalities. Dobutamine infusion, however, produced both thallium 201 defects and wall motion abnormalities in 100% of patients with coronary artery disease. The findings indicate the potential of pharmacological stress for MR, and both MR imaging and MR spectroscopy may find a clinical role in the assessment of patients with coronary artery disease.

Obituary

Professor C. B. Allsopp, MA, PhD, DSc

Cecil Benjamin Allsopp, Emeritus Professor of Physics Applied to Medicine at Guy's Hospital Medical School, died on October 16th, 1989, at the age of 85. He had played an important role in the affairs of the British Institute of Radiology, having been Editor of the Journal in the 1950s and President in 1963–64.

Professor Allsopp was an undergraduate at Emmanuel College, Cambridge, and went on to be a Research Assistant in the University Department of Physical Chemistry. There he worked on the refractive dispersion of various organic compounds and, in 1932, obtained his PhD. In 1934 he was co-author with F. W. Twyman of a book: *The Practice of Absorption Spectrophotometry with Hilger Instruments*. Subsequently he moved to the Department of Colloid Science and the Strangeways Laboratory, where he worked alongside Douglas Lea and became particularly interested in radiation chemistry and the action of radiation on living cells. In 1944 he published a comprehensive review of what was then known about radiochemical reactions, and in 1946 he contributed to an important conference in London, the proceedings of which were published as the first supplement to the BJR. This interest in radiation effects resulted in his appointment as a Lecturer in Physics at Guy's, where he succeeded to the Chair in 1953 and stayed until his retirement in 1970. He gained a DSc of the University of London in

1951.

The Department of Physics Applied to Medicine at Guy's had, under Professor Stead, developed an active role in the teaching of physics to medical students, and Professor Allsopp continued in this tradition. He helped revise and re-write Stead's widely-used A-level textbook *Elementary Physics* and, for many years, acted as an A-level examiner for the Oxford and Cambridge Schools Examination Board. Guy's Physics Department was also one of the first to devote a large part of its research effort to the physical aspects of diagnostic radiology and the limitation of doses received by patients undergoing diagnostic examinations.

Professor Allsopp had a great interest in the history of science and particularly in the history of the Institute and its Journal, as shown in his Presidential Address and his 1965 Silvanus Thompson Memorial Lecture. At the conversazione at Guy's during his presidential year, he persuaded Professor Stead to repeat the demonstration of Roentgen's original experiment discovering X-rays that he had first given in his Silvanus Thompson Lecture in 1959.

A less scientific event in his presidential year was the discovery that the front wall of the Institute's house (then 32 Welbeck St) was in a state of imminent collapse and had to be rebuilt. Needless to say, he coped with this crisis with his usual calm efficiency.

My first contact with Professor Allsopp was when I submitted my early papers to the Journal at the time he was Editor. As a very novice author, I found him most sympathetic and helpful. Later, as Non-Medical Secretary of the Institute during his presidential year, I saw at first hand his conscientiousness and close attention to detail and his ability to go quickly to the heart of a problem and find a solution. He was a good friend of the Institute and of Radiology.

JOHN HAYBITTLE

BIR ties

BIR ties are available to members at £5 each (£6 including post and packing). They are navy blue or maroon and carry the rays from the Institute's logo in gold. Please send a cheque payable to the BIR with the order.

Curt Westman Scholarship

Members wishing to visit the clinic in Vallingby, Sweden, of the late Dr Curt Westman, now owned by AB Medicinsk Rontgen, should write to the General Secretary of the BIR **before March 1 1990**. Return air fares and 2 weeks' accommodation are generously provided by AB Medicinsk Rontgen, and the BIR provides a sum towards expenses.

New BIR Members

Medical

Dr Brian Cosmann, MB, ChB, DMRD, ABR
(USA), Diagnostic Radiologist
Dr Ruth E. England, MB, BCh,BAO, MRCPI
(Manchester) Diagnostic Radiologist
Dr Rodney C. Goodfellow, MB, ChB, MFOM
(Preston, Lancs), British Nuclear Fuels plc
Dr Andrew J. Hails, MB, BS, MRCP
(Purfleet, Essex) Diagnostic Radiologist
Dr Martha W. A. Hewitson, MD, DMRD
(Broadstairs, Kent), Diagnostic Radiologist
Dr Shaun G. McGee, BA, MB, BS, MRCP
(London), Diagnostic Radiologist
Dr Niels Powell, FRCR, MB, BCh, DCH, DMRD
(Swansea), Diagnostic Radiologist
Dr William H. Ramsden, BM, FRCS
(Manchester), Diagnostic Radiologist
Dr John Rawlinson, MA, BM, BCh, FRCS, FRCR
(Southampton), Diagnostic Radiologist
Dr Christopher A. Rowland Hill, BA, MRCP
(London), Diagnostic Radiologist
Dr Joel C. Sim, MD
(Germany), Diagnostic Radiologist
Dr Prudencia N. M. Tyrrel, BA, MB, BCh, BAO, MRCPI
(Birmingham), Diagnostic Radiologist
Dr Katherine A. Vallis, MB, BS, MRCP, FRCR
(London), Radiotherapist/Oncologist
Dr Charles J. Wakeley, BSc, MB, BS, FRCS, FRCSEd
(Bristol), Diagnostic Radiologist
Mrs Trudi A. Wignall, MBChB, FRCS
(Manchester), Diagnostic Radiologist
Dr Robin Wood, MB, ChB, DIH, MFOM
(Seascale, Cumbria), British Nuclear Fuels plc
Dr Sylvia A. Worthy, MB, BS, MRCP
(Leeds), Diagnostic Radiologist

Non-Medical

Dr Siddick Abugrain, MSc
(Manchester), Physicist
Mr Frederick K. Bampton, BSc, MSc
(Knockholt, Kent) Physicist
Dr Johan G. E. A. Bierkens
(Manchester), Radiobiologist
Mr Gad Hochner,
(Watford), Elscint (GB) Ltd
Mr Fintan McEvoy, MVB, DUR, MRCUS
(Potters Bar, Herts), Veterinary Surgeon
Dr Trevor J. McMillan, BSc, PhD
(Sutton), Radiobiologist
Dr Thirupasundrie Padayachee, BSc, PhD
(London), Physicist
Mr David N. Prior, BSc, MSc
(Brighton), Physicist
Mr Graham J. Somerville
(St Albans), Polaroid UK Ltd
Mr Mark Thorn(Northampton),
Mallinckrodt Medical UK
Mr Bryan Womersley, Degree Photographic Science/MBA
(DuPont (UK) Ltd, Executive

Library News

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays).

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–7 p.m. and Thursdays 11 a.m.–5p.m. In her absence, assistance will be given by Miss Helen Smith. (Tel: 01-580 4085.)

The journal stock includes more than 100 titles. Although journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

Recent additions to the library

EDEN, A., 1988. Christian Doppler, thinker and benefactor.

LÜNING, M. & FELIX, R. (Eds), 1989. Abdomen. Komplexe bildgebende diagnostik.

NATIONAL RADIOLOGICAL PROTECTION BOARD, 1989. Living with radiation, 4th edn.

Hire of Institute facilities

Readers are reminded of the availability for hire of the Lecture Theatre, Foyer and Library. Affiliated societies are offered a discount.

The Lecture Theatre holds up to 100 people in raked seating and has excellent audio-visual equipment, including VHS video. The Foyer provides space for registration and refreshment breaks for 40 people. The Library, with its beautiful Adam ceiling, can accommodate up to 60 people for refreshment breaks or for an evening reception.

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

Quantification in imaging — what has it achieved and what is its future?
February 21, 1990
Chairmen: Drs R. Speller and W. Hately

Radiobiology proffered papers
February 23, 1990
All day work-in-progress meeting

Imaging towards 2000 — practical integration of new technologies
March 21, 1990
All day meeting at the Scientific Societies, London
Chairmen: Profs P. N. T. Wells and I. Isherwood
Speakers: R. Frakowiak, A. Hemingway, J. Howarth, W. R. Lees, H. Nunnerly, M. Smith and J. Williams

Conversazione
March 21, 1990
Royal College of Physicians, Regent's Park, London.
Lecture by Mrs Olivia Wilson on veterinary radiography.

Photodynamic therapy
April 4, 1990
Joint BIR/IPSM all day meeting organized by the BIR
Chairman: Dr D. Ash
Speakers: D. Ash, S. Bown, S. Brown, J. Colles, A. Mackenzie, W. Starr, J. Carruth and J. Lowdell

BIR Annual General Meeting
May 3, 1990 at 5 p.m.
36 Portland Place, London
BIR members only

The combination of chemotherapy and radiotherapy in clinical practice
May 10, 1990
All day meeting
Chairmen: Prof. A. Horwich, Dr J. Tobias and Dr S. Arnott
Speakers: G. G. Steel, A. Timothy, M. Brada, P. Hoskin, N. Plowman, P. Blake, J. R. Yarnold, D. P. Dearnaley, D. Spooner, D. Tait and N. Bleehen

The repair of radiation damage — molecules to man
May 11, 1990
All day work-in-progress meeting

Radiology 90

Harrogate, 11-13 June 1990

Call for work-in-progress abstracts

The deadline for receipt of proffered abstracts for work-in-progress is 15 April 1990. Please contact the Conference Office for an abstract form.

BIR Conference Services

Is there a seminar, conference or evening get-together you want to organize, but you don't have the time? The BIR Conference Office may be able to help you. Please call Nelleke van Helfteren, Conference Manager, to discuss possibilities.

01-580 4085

Product news

First Clinac 2500C at Orlando, Florida

Varian have announced the installation of the first Clinac 2500C linear accelerator, said to be the most powerful and penetrating commercially available X-ray beam for administering radiation therapy. The unit's 24 million volt beam can penetrate the patient to treat deep-seated tumours that lower energy accelerators cannot reach as effectively.

The Clinac 2500C accelerator's unique switched-guide design also provides low energy 6 MV X rays and a range of electron energies from 6 million volts (MeV) to 22 MeV, giving the radiation oncologist the clinical flexibility to treat a wider variety of cancer types.

Standard with the accelerator is the C-Series Extended Travel Range treatment couch which works under computer control to produce precision positioning for a wide range of clinical treatment fields. Large fields can be treated at extended distances without requiring patient repositioning which assists clinicians in performing more accurate and reproducible treatment setups.

For further information contact Varian International AG, Kollerstrasse 38, CH-6300 Zug, Switzerland.

Interventional Ultrasound System

Diasonics Sonotron have introduced a sophisticated interventional ultrasound imaging system designed to perform high resolution 360° real-time sector imaging of the peripheral vascular system and other lumina of the body. The combination of high speed computer processing with ultra high frequency imaging capability enables the visualization of structural detail undetectable by conventional ultrasound technology.

The development is the result of a joint venture between Diasonics and the Boston Scientific Corporation which manufactures Medi-tech, Mansfield and Microvasive products.

For further information contact Diasonics Sonotron on 0234 40881.

Gas Delivery System from Victoreen

The Victoreen Model 8301 Gas Delivery System, as shown at the RSNA Show in November, provides for automatic collection of radioactive gas, monitoring of the activity of the gas and delivery of the gas to the patient for the purpose of Positron Emission Tomography (PET) studies. The system features user-selectable Bolus or Continuous Mode gas delivery and is designed to protect the patient and operator in the event of a malfunction.

Victoreen Inc is a major international supplier of microprocessor based nuclear instruments and radiation monitoring systems.

For further information contact Margaret Meek, Marketing Services Manager, Victoreen Inc, 6000 Cochran Road, Cleveland, Ohio 44139-3395, USA.

Princess opens new CT Scanner Suite

HRH Princess Michael of Kent listens to Brian Goldthorpe (L) from 3M Medical Imaging Systems explaining the 3M Laser Imager Plus System recently installed at Watford District General Hospital. The system is linked to the Siemens Somatom HiQ Scanner. Also in the picture are Brian Brandon of 3M (R) and John Fitzpatrick (background), the District Radiographer.

RadCare from CHC

Computer Health Computing have appointed Roger Bowden as a consultant to their Sales and Marketing team with the main task of launching their Radiology information system, RadCare, in the UK. This medical imaging computer system, which provides options for digital radiology/PACS, optical disc storage and voice recognition, has already been installed in several large hospitals in the USA.

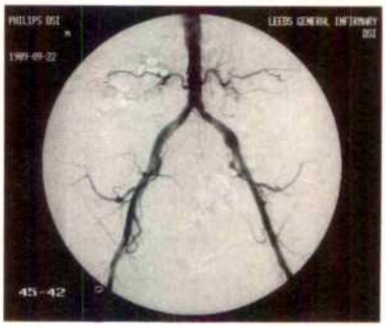
For further information contact Dr John Ironmonger, CHC (UK) Ltd, Origo Centre, Research Park Avenue North,

Redevelopment of Manchester Royal Infirmary

Philips Medical Systems have recently been awarded a contract for the development of ten X-ray rooms in the Imaging Department linked to a district-wide Radiology Information System at Manchester Royal Infirmary.

As part of the project they will supply a Radiology Information System (RADOS) designed to meet the needs of the hospital's Radiology Department and provide comprehensive Electronic Data Processing to support the hospital. They are also supplying three of the latest Philips Digital Spot Imaging Systems (DSI). The main advantages of this new system are the immediate availability of high-quality images during the examination procedure and real-time digital processing to enhance the diagnostic value of images.

The digital image data acquired is suitable for digital archiving and communication which together with the RADOS system is compatible with the Radiology Department's aim of becoming a "filmless" Department within the next five years.



DSA of the iliac artery

Stereotactic radiosurgery system

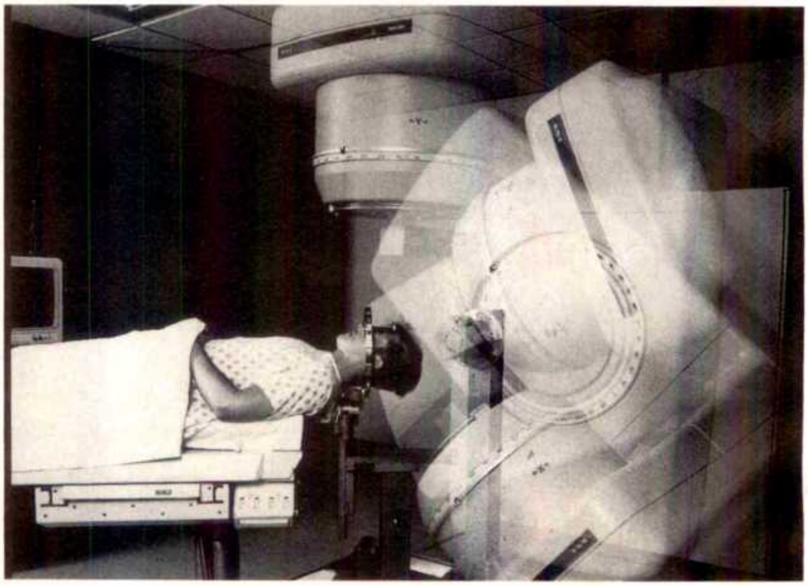
Philips Medical Systems have introduced a device for non-surgical treatment of lesions in the brain with the same degree of accuracy as the "gamma knife", but with a more sophisticated computer technology for easier set-up and faster treatment dose planning. Arteriovenous malformations are the most common lesions treated with this technique. However, the system has the flexibility to treat conventional radiotherapy patients where pin-point accuracy is essential, for example with tumours of the spinal cord, as well as small lesions confined to a localized area.

Most patients can be treated on a one-day, out-patient basis, as once the lesion has been located and the optimum treatment plan computed, the preparation of the patient and the treatment takes about 20–30 minutes.

The system is an extension to a standard linear accelerator such as those used by most hospitals for radiation therapy cancer treatment. It consists of an isocentric sub-system used in conjunction with a very powerful dedicated 3D planning system and stereotactic equipment.

Previously this type of treatment was only available at large institutions using multiple cobalt radiation sources, but now this technology is within the reach of community hospitals because of the lower cost.

For further information contact Philips Medical Systems, PO Box 10000, 5680 DA Best, The Netherlands.



BIR Company Subscribers

The BIR company subscriber scheme is aimed at all companies who advertise in the BJR or exhibit at the MED X RAY technical exhibition. For a subscription of £250 p.a. for an initial period of 3 years, an attractive package of benefits is offered (see March 1988 Bulletin for details).

If your company is interested in joining the scheme, please contact Mr Tony Hudson, Administration Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT. Tel: 01-580 4085. Companies that have enrolled to date are listed below.

Agfa-Gevaert Ltd
27 Great West Road, Brentford, Middlesex TW8 9AX; tel. 01-560 2131. Product Areas 1. Contact Mr G. Mountford, Director.

Amersham International PLC
Lincoln Place, Green End, Aylesbury, Bucks HP20 2TP; tel. 0296-395222. Product areas 4, 5, 6. Contact Mr James McLaughlin, Sales and Marketing Manager.

British Nuclear Fuels plc
Room 525, Hinton House, Risley, Warrington, Cheshire WA3 6AS; tel. 0925-835022. Product areas 8, 11. Contact Dr R. J. Berry, Director of Health and Safety and Environmental Protection.

Cardiac Services Ltd
95A Finaghy Road, South Belfast BT10 OBY; tel. 0232-625566. Product areas 1, 3, 4, 5, 6. Contact Mr R J Brown, Managing Director.

Central Electricity Generating Board
15 Newgate Street, London EC1A 7AU; tel. 01-634 6898. Product areas 7, 8. Contact Mr R. V. Brierley, Office Services Manager.

Du Pont (UK) Ltd
Wedgwood Way, Stevenage, Hertfordshire SG1 4QN; tel. 0438 734000. Product areas 1, 3, 4, 5, 6, 7, 9 and 10. Contact Mr E. G. Lovat, Product Manager, Diagnostic Imaging.

E. G. & G. Astrophysics Research Ltd
Vale Road, Windsor, Berkshire SL4 5JP; tel. 0753-855611. Product areas 1, 6, 7, 8,. Contact Miss Susan Holgate, Sales Executive (Therapy).

Elscint (GB) Ltd
Tower Road, Berinsfield, Oxfordshire OX9 8LW; tel. 0865-340900 . Product areas 1, 3, 4. Contact Ms Faith Gorman, Managing Director.

E-Z-EM Ltd
1230 High Road, Whetstone, London N20; tel. 01-446 9714. Product areas 1, 2, 8. Contact Mr D. F. Wills, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London NW3 6JH; tel 01-586 9351. Product areas 1, 3. Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
4 Clarendon Chambers, Clarendon Street, Nottingham NG1 5LN; tel. 0602-483807. Product areas 1, 3, 4, 5, 6. Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks SL1 4ER; tel. 0753-874000. Product areas 1, 3, 4, 5, 6, 8. Contact Mr Jack Strange, Sales Administration.

Kodak Ltd
PO Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU; tel. 0442-61122. Product areas 1. Contact Mr P. E. Blackwell, Manager, Health Sciences Division.

3M UK PLC
3M House, Bracknell, PO Box 1, Berks RG12 1JU; tel. 0344 426726. Product areas 1. Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ. tel. 0604-46132. Product areas 4, 5. Contact Mr D. G. L. Wood, Business Manager.

Medical XraySupplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU; tel. 01-205 9500. Product areas 1. Contact Mr R. J. Laird, Sales Director/Managing Director.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA; tel. 516-741 7614. Product areas 1, 3, 4, 5, 6, 8. Contact Mr H. Glasser, General Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA; tel. 021-742 2444. Product areas 1, 3. Contact Mr L. Birch Hansen, Managing Director.

Philips Medical Systems
Kelvin House, 63-75 Glenthorne Road, Hammersmith, London W6 OLJ; tel. 01-741 1666. Product areas 1, 3–8. Contact J. M. Woolston, Sales and Marketing Manager.

Polaroid (UK) Ltd
Ashley Road, St Albans, Herts AL1 5PR; tel. 0727 59191. Product areas 1, 3. Contact Ms Tina Thompstone, Product Supervisor.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR; tel. 09277-67433/63320. Product areas 8. Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA; tel. 0635-32222. Product areas 2, 10. Contact Mr Christopher Trim, Publicity Officer.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE; tel. 04446-6011. Product areas 1, 2, 3. Contact Mr A. Greaves, Product Manager.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands; tel. 015 61 0121. Product areas 1, 6. Contact Mr. P Blonk, Office Manager, X-ray BU.

Wardray Products Ltd
Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP; tel. 01-398 9911. Product areas 8. Contact Mr R. B. Wardley, Managing Director.

Key to product areas:

1. Diagnostic X-ray inc. NMR and CT.
2. Interventional radiology.
3. Ultrasound.
4. Nuclear medicine.
5. Radiopharmaceuticals.
6. Radiotherapy and oncology.
7. Radiobiology.
8. Radiation protection.
9. PACS.
10. Image processing.
11. Nuclear fuel cycle services.

Meetings and Courses

International Symposium in Physics of Medical Imaging and Advances in Computer Applications
February 21–23, 1990
New Delhi, India
Further details: Dr M. M. Rehani, Organizing Secretary, ISPMICA, Medical Physics Unit, IRCH, All India Institute of Medical Sciences, New Delhi-110029, India.

Theoretical Course on Obstetric Ultrasound
March 26–30, 1990
London
Further details: The Postgraduate Education Office, The Royal College of Obstetricians and Gynaecologists, 27 Sussex Place, Regent's Park, London NW1 4RG. Tel: 01-262 5425.

The Sixth Midlands Course in Otoradiology and MRI in ENT
April 19–21, 1990
Coventry
Further details: Miss M. Adams, Centre Administrator, Warwickshire Postgraduate Medical Centre, Stoney Stanton Road, Coventry CV1 4FG.

Advanced Oncology: Urological Cancer
April 27–28, 1990
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London W1M 3DG. Tel: 01-262 5425.

Success and Creativity in Pharmaceutical Research and Development
April 30–May 1, 1990
London
Further details: Renata Duke, IBC Technical Services Ltd, Bath House (3rd Floor), 56 Holborn Viaduct, London EC1A 2EX.

Euroson 90
7th Congress of the European Federation of Societies for Ultrasound in Medicine and Biology
May 6–11, 1990
Jerusalem, Israel
Further details: The Secretariat, PO Box 50006, Tel-Aviv 61500, Israel. Tel: 03 654571. Extended abstract deadline: January 31, 1990.

Pulsed Lasers in Angioplasty: International Workshop
May 11–12, 1990
Tübingen, West Germany
Further details: K. R. Karsch, Department of Cardiology, Medical Clinic, University of Tuebingen, Otfried-Müller-Str. 10, D-7400 Tübingen, FRG

27th Congress of the European Society of Paediatric Radiology
May 14–19, 1990
Munich, West Germany
Further details: Dr H. Fendel, Universität Kinderklinik, Röntgenabteilung, Lindwurmstr. 4, D-8000 München 2, FRG. Tel: 089 5160 3102.

Blood Vessel Imaging Using Ultrasound Techniques
May 16–18, 1990
Southampton
Further details: Mr K. N. Humphries, Blood Vessel Imaging Course, 10 Swale Drive, Chandlers Ford, Hampshire SO5 3QY.

Bisphosphonates: Current status and future prospects
May 21–22, 1990
London
Further details: Renata Duke, IBC Technical Services Ltd, Bath House (3rd Floor), 56 Holborn Viaduct, London EC1A 2EX.

Liver Imaging: Past and Future Trends in MRI and CT
June 25–27, 1990
Boston, USA
Further details: Joseph T. Ferrucci, Department of Continuing Education, Harvard Medical School, Boston, MA 02115, USA. Tel: 617 732-1525

Brachytherapy Working Conference 6th International Selectron Users' Meeting
September 9–11, 1990
Florence, Italy
Further details: Conference Secretariat, Nucletron International B. V., PO Box 110, 3956 ZT Leersum, The Netherlands. Tel: 31 0 3434 54224.

International Skeletal Society — 17th Annual Refresher Course
September 9–15, 1990
Salzburg, Austria
Further details: Secretary/Treasurer, International Skeletal Society, Radiology Department, Hospital of the University of Pennsylvania, 3400 Spruce Street, Philadelphia PA19104, USA.

Muscoskeletal Disorders
September 12–15, 1990
Salzburg, Austria
Further details: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: 404 641-9773.

Interventional Radiology
September 19–21, 1990
Istanbul, Turkey
Further details: Marmara University Medical School, Haydarpasa, Istanbul, Turkey. Abstract deadline: April 1, 1990.

Training and Qualifications in Radiation Protection
October 2, 1990
London
Further details: Dr D. N. S. Dixon, Programme Committee Secretary, The Society for Radiological Protection, 67 Oatlands Park, Linlithgow, West Lothian EH49 6AS. Tel: (031) 244 2779.

Riyadh Armed Forces Hospital Third International Course on Magnetic Resonance Imaging
October 14–17, 1990
Riyadh, Saudi Arabia
Further details: Department of Medical Studies, Armed Forces Hospital, PO Box 7897, Riyadh 11159, Kingdom of Saudi Arabia. Tel: 9661 477 7714, Ext. 2289/2269

6th World Congress in Ultrasound
September 1–6, 1991
Copenhagen, Denmark
Further details: Torben Larsen, Department of Gynecology, Herlev Hospital, DK-2730 Herlev, Denmark.

European Congress of Radiology '91
September 15–20, 1991
Vienna, Austria
Further details: The Congress Secretariat ECR '91, c/o Vienna Academy of Postgraduate Medical Education and Research, Alser Straße 4, A-1090 Vienna, Austria

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR Bulletin.

Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.

BIR Bulletin

Honorary Editor, BIR Bulletin: D. Rickards, LRCP, MRCS, FFR(D)SA, FRCR
Please address all correspondence to: Honorary Editor, BIR Bulletin, The British Institute of Radiology,
36 Portland Place, London W1N 4AT

The British Institute of Radiology is not responsible for opinions expressed in the BIR Bulletin

Radiology 90

Radiology 90 News Update

Harrogate, 11-13 June 1990

The Scientific Programme Committee met in January to select the proffered presentations to be included in the sessions at Radiology 90. There was a record number of proffered abstracts this year and the Committee has put together a full and interesting programme of over 240 presentations to span the three days of the Congress. The full programme is being printed now and will be available at the end of March. It will be sent out to all members with the April Bulletin, so if you have not already done so, you can reserve your place knowing exactly what highlights will be on offer.

Registration: there are still a few places left, so fill in a registration form as soon as possible, as they are going fast.

Med X Ray, the technical trade exhibition is progressing very well, with over 80 companies having booked space and more showing interest. A list of attending companies will be included in the final programme for Radiology 90, so that you can plan your visits to MED X RAY at the same time as deciding which scientific sessions to attend.

The Harrogate International Conference and Exhibition Centre

An overview of both the status and potential of radiobiological modelling at Radiology 90

"The current status of radiobiological modelling", a review lecture by Dr Roger Dale from the Charing Cross Hospital, London, will be the starting point for a session on **Oncology** on Tuesday 12 June in the afternoon.

The review lecture will focus on the developments in this field which have taken place in the last decade and which are introducing some interesting pointers as to the way radiotherapy treatments might progress in the future. The new radiobiological ideas can provide a useful new mechanism for examining all the main types of radiotherapy, and also highlight areas on which further quantitative information is needed.

IAEA research funding

Members may like to know that the International Atomic Energy Agency runs a scheme for supporting research, particularly aimed at the needs of developing countries, in the fields of Nuclear Medicine, Applied Radiation Biology and Radiotherapy and Radiation Dosimetry. Details and application forms are available from Mr Ian Bulmer, Department of Energy, Atomic Energy Division, 1 Palace Street, London SW1E 5HE, and they should be returned to him by 16 March. (Apologies for the short notice but details have only just ben received by the BIR.)

Health services' use of ionising radiation

Health Service Managers received this Health Circular [HC(89)18] in December 1989. In many cases, it has been passed to radiation protection advisers for a response to be formulated. The Health Circular requires that authorities respond to their regional health authorities by February and they in turn are required to respond to the Department of Health by March 1990. Since no guidance is given as to the exact form which any response should take, the Radiation Protection Committee of the BIR offers the following comments for the benefit of members.

Essentially, the Health Circular lists three requirements.

(1) To review the management of all departments making use of ionising radiations (including radioactive substances) to ensure they conform with the statutory requirements and the guidance on good practice referred to in this circular.

(2) To confirm that they have reviewed their procedures in the light of this circular and corrected any deficiencies:

(i) districts should send a report to their region, and Special Health Authorities a report to the Department by February 1990;

(ii) regions (on behalf of their districts) should send a summary report to the Department of Health by March 1990.

(3) To establish a system to review and update periodically their procedures in the light of changing guidance, and to report the main features of this system in the timescale given in (2) above.

While a detailed response from members in district health authorities would not be appropriate, we consider that sufficient information should be made available through management to Regional Scientific Officers to enable them to formulate their response.

RSOs are unlikely to want detailed information relating, for example, to individual X-ray rooms, but will need to know details of situations where the degree of non-compliance is likely to attract the attention of inspectors of the Health and Safety Executive, radiochemical inspectors or of a new inspectorate set up by the Department of Health.

Members may wish to take advantage of the opportunity offered in their responses to examine the role of management, to analyse the responsibility of management in ensuring that the requirements of the Regulations and Statutory Instruments are being fulfilled, and to check that these responsibilities are being discharged, particularly in respect of the Ionising Radiations (Protection of persons undergoing diagnosis or treatment) Regulations 1988; Statutory Instrument No 778 of 1988.

DEREK GIFFORD
January 1990

Library News

The BIR Library is open weekdays 9 a.m.–5 p.m. (7 p.m. on Tuesdays).

The Librarian, Mrs Gunnel Ingham, is in attendance Tuesdays 11 a.m.–7 p.m. and Thursdays 11 a.m.–5p.m. In her absence, assistance will be given by Miss Helen Smith. (Tel: 01-580 4085.)

The journal stock includes more than 100 titles. Although journals may not be taken out of the library, there is a photocopy service, also available by post or FAX. A list of current journals is available on request and is also published in the March and September issues of the Bulletin. Most books (except the historical collection) are available on loan.

Current journals held in the Library

Acta Oncologica
Acta Radiologica
American Journal of Neuroradiology
American Journal of Roentgenology
Annales de Radiologie (France)
Annals of Nuclear Medicine (Japan)
Annals of the ICRP
Applied Health Physics, Abstracts and Notes
Applied Radiation and Isotopes
Astro Newsletter
Australasian Radiology
BMUS Bulletin
British Journal of Radiology
British Medical Bulletin
British Medical Journal
British Society of Dental and Maxillofacial Radiology Newsletter
BSI News
Cancer
Cancer Research
Cancer Research Campaign Annual Report
Cancer Treatment Reviews
Cardiovascular and Interventional Radiology
Cell and Tissue Kinetics

Chinese Journal of Nuclear Medicine
Chinese Journal of Radiology
Clinical Imaging
Clinical Nuclear Medicine
Clinical Oncology
Clinical Physics and Physiological Measurement
Clinical Radiology
Computerized Medical Imaging and Graphics
Current Contents (Life Sciences)
Current Opinion in Radiology
Current Problems in Diagnostic Radiology
Diagnostic Imaging (USA)
Diagnostica per Immagini (Italy)
Egyptian Journal of Radiology and Nuclear Medicine
European Journal of Cancer and Clinical Oncology
European Journal of Nuclear Medicine
European Journal of Radiology
European Journal of Surgical Oncology
Excerpta Medica. 14 Radiology
Gastrointestinal Radiology
HPA Bulletin
Health Physics
IAEA Newsbriefs
ICRU News
ISRRT Newsletter
Indian Journal of Radiology and Imaging
International Journal of Hyperthermia
International Journal of Radiation Biology
International Journal of Radiation Oncology, Biology , Physics
Investigative Radiology
Journal Belge de Radiologie
Journal de Radiologie (France)
Journal Européen de Radiotherapie
Journal of Clinical Oncology
Journal of Computer Assisted Tomography
Journal of Interventional Radiology
Journal of Medical Imaging
Journal of Nuclear Medicine
Journal of Radiological Protection
Journal of the Canadian Association of Radiologists
Journal of The National Cancer Institute
Journal of The Royal Society of Medicine
Journal of Thoracic Imaging
Journal of Ultrasound in Medicine
Lancet
Magnetic Resonance in Medicine
Medical Physics
Medical Radiography and Photography
Meditsinskaya Radiologiya (USSR)
Neuroradiology
Nuclear Medicine and Biology
Nuclear Medicine Communications
Pediatric Radiology
Physics in Medicine and Biology
Proceedings of The American Association for Cancer Research
Proceedings of the American Society of Clinical Oncology
Rad
Radiation Protection Dosimetry
Radiation Research
Radiatsionnaya Biologiya (USSR)
Radiographics
Radiography Today
Radiologia Medica (Italy)
Radiologic Clinics of North America
Radiological Protection Bulletin
Radiology
Radiology Now
Radiotherapy and Oncology
Rays
Rivista di Radiologia (Italy)
RöFo (Germany)
Seminars in Interventional Radiology
Seminars in Nuclear Medicine
Seminars in Roentgenology
Seminars in Ultrasound, CT and MR
Skeletal Radiology
Strahlentherapie und Onkologie
Ultrasonics
Ultrasound in Medicine and Biology
Urologic Radiology
Yearbook of Diagnostic Radiology

Recent additions to the library

Bentel, G. C., Nelson, C. E. & Noell, K. T., 1989. Treatment planning and dose calculation in radiation oncology. 4th edn.

Callen, P. W. (Ed.), 1988. Ultrasonics in obstetrics and gynaecology. 2nd edn.

Commission of the European Communities, 1988. Radiation protection optimization "Advances in practical implementation". Proceedings.

Faulkner, K. & Wall, B. F. (Eds), 1988. Are X-rays safe enough — patient doses and risks in diagnostic radiology (IPSM).

Felix, W. R. Jr (Ed.), 1988. Non-invasive diagnosis of peripheral vascular disease.

Fleischer, A. C. & James, A. E. (Eds), 1989. Diagnostic sonography — principles and clinical applications.

IAEA & WHO, 1987. Dosimetry in radiotherapy. Vol. 1–2. Proceedings.

Newton, T. H., Hasso, A. N. & Dillon, W. P. (Eds), 1988. CT of the head and neck. (Modern neuroradiology, Vol. 3.)

Siegel, M. J. (Ed.), 1988. Contemporary issues in computed tomography. Pediatric body CT.

Stoll, B. (Ed.), 1988. Cost versus benefit in cancer care.

Straub, W. H. (Ed.), 1989. Manual of diagnostic imaging. A clinician's guide to clinical problem solving. 2nd edn.

Suslick, K. S. (Ed.), 1988. Ultrasound — its chemical, physical and biological effects, 1988.

Withers, H. R. & Peters, L. J. (Eds), 1988. Innovations in radiation oncology.

Yoder, I. C., 1988. Hysterosalpingography and pelvic ultrasound: imaging in infertility and gynaecology.

Use of RSM Library

BIR members might be pleased to know that there is an agreement which allows limited use of the RSM library for reference purposes, including photocopying and searches.

Members should apply to the BIR librarian, Mrs Gunnel Ingham, for a visitor's card.

New BIR Members

Medical

Dr Daniel I. Boxer, BSc, MB, BS, MRCP, FRCR
(London) Diagnostic Radiologist
Dr Mair Critchley, MB, BS, MD, FRCR
(Liverpool) Consultant in Nuclear Medicine
Dr Ann Mary M. Jones, BSc, MB, BS, MRCP
(Bristol) Diagnostic Radiologist
Dr Susan King, MB, ChB, MRCP, FRCR Part 1
(London) Diagnostic Radiologist
Dr Ekaterini Kyriacou, MB, BS, MRCP
(London) Diagnostic Radiologist
Dr Rita McAvinchey, MB, BS, MRCP
(London) Diagnostic Radiologist
Dr Paul M. G. McIlroy, MB, BCh, BAD, MRCP
(Manchester) Diagnostic Radiologist
Dr Mahesh K Sketty, MD, DMRD
(Dublin) Diagnostic Radiologist
Dr Sathi A. Sukumar, MB, MS, MRCP
(Manchester) Diagnostic Radiologist

Non-medical

Mr William A. Heywood, BSc, MSc, MIPSM
(Dorset) Physicist
Mr Eduard Klarich
(Fuji Photo Film Ltd) Executive
Mr James McLaughlin, BSc
(Amersham International PLC) Executive
Miss Moira Reidy, BBS
(Fuji Photo Film Ltd) Marketing Manager
Miss Anna C. Shores, BA(Hons), Dip M
(Bard Ltd) Product Manager
Dr Andrew Todd-Pokrapek, BA,MPhil
(London) Physicist
Mr Simon M. Weeden
(Toshiba Medical Systems Ltd) Executive
Ms Ann L. Wood, DCR(T), HDCR, MDCR
(Abu Dhabi) Radiographer

Change of venue

Please note that the BIR Conversazione on Wednesday, 21 March, 1990 is going to be held at The Royal Institution, 21 Albemarle Street, London instead of the Royal College of Physicians, as previously advertised.

Members' use of the Siemens Room

Members may borrow the Siemens Room free of charge, subject to availability. This conference meeting room seats 16 people with comfort.

Full details from Mr Anthony Hudson, Administration Manager.

BIR Calendar

Unless otherwise indicated, enquiries about the following events should be addressed to the Conference Manager, British Institute of Radiology, 36 Portland Place, London W1N 4AT (Tel. 01-580 4085).

Imaging towards 2000 — practical integration of new technologies
March 21, 1990
All day meeting at the Scientific Societies, London
Chairmen: Profs P. N. T. Wells and I. Isherwood
Speakers: R. Frakowiak, A. Hemingway, J. Howarth, W. R. Lees, H. Nunnerly, M. Smith and J. Williams

Conversazione
March 21, 1990, 6.15 – 9.30 p.m.
Royal Institution, Albemarle Street, London.
The lecture is by Mrs Olivia Wilson on veterinary radiography: "Aardvarks, apes and alligators — ultrasound and X-ray at London Zoo"

Photodynamic therapy
April 4, 1990
Joint BIR/IPSM all day meeting organized by the BIR
This meeting has been generoulsy sponsored by Lederle Laboratories and Oxford Lasers Ltd.
Chairman: Dr D. Ash
Speakers: D. Ash, S. Bown, S. Brown, J. Colles, A. Mackenzie, W. Starr, J. Carruth and J. Lowdell

BIR Annual General Meeting
May 3, 1990 at 5 p.m.
36 Portland Place, London
BIR members only

The combination of chemotherapy and radiotherapy in clinical practice
May 10, 1990
All day meeting
Chairmen: Prof. A. Horwich, Dr J. Tobias and Dr S. Arnott
Speakers: G. G. Steel, A. Timothy, M. Brada, P. Hoskin, N. Plowman, P. Blake, J. R. Yarnold, D. P. Dearnaley, D. Spooner and D. Tait

The repair of radiation damage — molecules to man
May 11, 1990
All day work-in-progress meeting

Radiology 90

Harrogate, 11-13 June 1990

Call for work-in-progress abstracts

The deadline for receipt of proffered abstracts for work-in-progress is 15 April 1990. Please contact the Conference Office for an abstract form.

BIR Conference Services

Is there a seminar, conference or evening get-together you want to organize, but you don't have the time? The BIR Conference Office may be able to help you. Please call Nelleke van Helfteren, Conference Manager, to discuss possibilities.

01-580 4085

BIR Company Subscribers

The BIR company subscriber scheme is aimed at all companies who advertise in the BJR or exhibit at the MED X RAY technical exhibition. For a subscription of £250 p.a. for an initial period of 3 years, an attractive package of benefits is offered.

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British Nuclear Fuels plc
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1230 High Road, Whetstone, London N20; tel. 01-446 9714. Product areas 1, 2, 8. Contact Mr D. F. Wills, Sales and Marketing Manager.

Fuji Photo Film (UK) Ltd
125 Finchley Road, London NW3 6JH; tel 01-586 9351. Product areas 1, 3. Contact Mr R. G. Brown, Marketing and Administration Manager.

Gammex-RMI Ltd
4 Clarendon Chambers, Clarendon Street, Nottingham NG1 5LN; tel. 0602-483807. Product areas 1, 3, 4, 5, 6. Contact Miss Eileen Parr, Commercial Manager.

IGE Medical Systems Ltd
352 Buckingham Avenue, Slough, Berks SL1 4ER; tel. 0753-874000. Product areas 1, 3, 4, 5, 6, 8. Contact Mr Jack Strange, Sales Administration.

Kodak Ltd
PO Box 66, Station Road, Hemel Hempstead, Herts HP1 1JU; tel. 0442-61122. Product areas 1. Contact Mr P. E. Blackwell, Manager, Health Sciences Division.

3M UK PLC
3M House, Bracknell, PO Box 1, Berks RG12 1JU; tel. 0344 426726. Product areas 1. Contact Mr Alan Budge, Marketing Manager.

Mallinckrodt Diagnostica (UK) Ltd
11 North Portway Close, Round Spinney, Northampton NN3 4RQ. tel. 0604-46132. Product areas 4, 5. Contact Mr D. G. L. Wood, Business Manager.

Medical XraySupplies Ltd
Unit 12, Kingsbury Industrial Estate, Church Lane, Kingsbury, London NW9 8AU; tel. 01-205 9500. Product areas 1. Contact Mr R. J. Laird, Sales Director/Managing Director.

Nuclear Associates
100 Voice Road, Carle Place, New York 11514-1593, USA; tel. 516-741 7614. Product areas 1, 3, 4, 5, 6, 8. Contact Mr H. Glasser, General Manager.

Nucletron Trading Ltd
Nucletron House, Tarporley Business Centre, Tarporley, Cheshire, CW6 9UY; tel: 0829 733611. Product areas 6, 8. Contact Mrs Marilyn A. Hart, Office Manager.

Nycomed (UK) Ltd
Nycomed House, 2111 Coventry Road, Sheldon, Birmingham B26 3EA; tel. 021-742 2444. Product areas 1, 3. Contact Mr L. Birch Hansen, Managing Director.

Philips Medical Systems
Kelvin House, 63–75 Glenthorne Road, Hammersmith, London W6 OLJ; tel. 01-741 1666. Product areas 1, 3–8. Contact J. M. Woolston, Sales and Marketing Manager.

Polaroid (UK) Ltd
Ashley Road, St Albans, Herts AL1 5PR; tel. 0727 59191. Product areas 1, 3. Contact Ms Tina Thompstone, Product Supervisor.

Premise Engineering Ltd
Tibbs Hill Road, Abbots Langley, Watford, Herts WD5 ODR; tel. 09277-67433/63320. Product areas 8. Contact Mr R. K. Beach, Director.

Quantel Ltd
Administration Centre, Kiln Road, Newbury, Berkshire RG13 2HA; tel. 0635-32222. Product areas 2, 10. Contact Mr Christopher Trim, Publicity Officer.

Schering Health Care Ltd
The Brow, Burgess Hill, West Sussex RH15 9NE; tel. 04446-6011. Product areas 1, 2, 3. Contact Mr A. Greaves, Product Manager.

Toshiba Medical Systems Europe BV
Schieweg 1, 2627 An Delft, The Netherlands; tel. 015 61 0121. Product areas 1, 6. Contact Mr. P Blonk, Office Manager, X-ray BU.

Wardray Products Ltd
Hampton Court Estate, Summer Road, Thames Ditton, Surrey KT7 OSP; tel. 01-398 9911. Product areas 8. Contact Mr R. B. Wardley, Managing Director.

Key to product areas:

1. Diagnostic X-ray inc. NMR and CT.
2. Interventional radiology.
3. Ultrasound.
4. Nuclear medicine.
5. Radiopharmaceuticals.
6. Radiotherapy and oncology.
7. Radiobiology.
8. Radiation protection.
9. PACS.
10. Image processing.
11. Nuclear fuel cycle services.

Meetings and Courses

A 4-day Introductory Training Course in Parallel Computing
March 26–30, 1990
London
Further details: The Research Support Officer, Centre for Parallel Computing , University of London, Queen Mary and Westfield College, Mile End Road, London E1 4NS. Tel: 01 975 5167.

72nd Annual Meeting of the American Radium Society
April 21–25, 1990
Scottsdale, Arizona
Further details: Ms Suzanne Bohn, Administrative Director, American Radium Society, 1101 Market Street, 14th Floor, Philadelphia, PA 19107, USA.

Impact of Personal Computers on Radiation Oncology Departments 4th Workshop of the European Association of Radiology Commission Informatique
April 23–25, 1990
Geneva, Switzerland
Further details: Dr P. Minet, Service de Radiothérapie, CHU Sart-Tilman, 4000 Liege, Belgium. Tel: 041-30 71 11.

5th International Symposium on Diagnostic Imaging
April 23–27, 1990
Barcelona
Further details: Nuria de Arana, c/o Centro Radiologico Computarizado de Barcelona, Tavern 82, 08006 Barcelona, Spain.

Advanced Oncology: Urological Cancer
April 27–28, 1990
London
Further details: The Conference Office, The Royal College of Radiologists, 38 Portland Place, London W1M 3DG. Tel: 01-262 5425.

British Nuclear Energy Society Conference on Occupational Exposure
April 29–May 3, 1990
Guernsey, Channel Islands
Further details: Mr G. A. M. Webb, National Radiological Protection Board, Chilton, Didcot, Oxon OX11 ORQ. Tel: 0235 833891.

Biliary Calculus Disease: Current Concepts in Diagnosis and Management
May 7–9, 1990
Boston, USA
Further details: Paula F. DeLong, Harvard Medical School, Massachusetts General Hospital, Boston, Massachusetts 02114, USA.

Diagnostic Imaging in Musculo-Skeletal Radiology
May 10–11
Glasgow
Further details: The Honorary Secretary,Royal College of Physicians & Surgeons of Glasgow, 242 St Vincent Street, Glasgow G2 5RJ. Tel: 041 221 6072

Cardiovascular and Interventional Radiological Society of Europe and American Society of Cardiovascular and Interventional Radiology Joint Meeting and Postgraduate Course
May 13–18, 1990
Brussels, Belgium
Further details: Conference Services, 3 Avenue de l'Observatoire, Box 17, B-1180 Brussels, Belgium. Tel: 32 2 375 16 48.

Hyperthermia in Clinical Oncology
May 18–19, 1990
Noordwijk aan Zee, The Netherlands
Further details: G. van den Bos, Dr Daniel den Hoed Cancer Center, Department of Hyperthermia, Groene Hilledijk 301, NL-3075 AE Rotterdam, The Netherlands.

CT and MR in Body Imaging: a Comprehensive Course
May 22–25, 1990
California, USA
Further details: Radiology Postgraduate Education, University of California, 521 Parnassus Avenue, Room C-324, San Francisco, CA 94143, USA. Tel: (415) 476 5731.

Systemic and Regional Hemodynamics in Liver Diseases
IBMI 6th International Symposium
June 3–5, 1990
Further details: Dr C. Sabbà,MD, Scientific Secretary, Institute of Clinica Medica I, University of Bari, Policlinico Piazza G. Cesare,70124 Bari, Italy. Tel: 39-80-5227796.

Radiology in Scandinavia and the Soviet Union
June 16–30
California, USA
Further details: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, GA 30077-1925. Tel: 404 641-9773.

XIV Symposium Neuroradiologicum
June 17–23, 1990
London
Further details: Conference Associates NSL, Congress House, 55 New Cavendish Street, London W1M 7RE. Tel; 01-486 0531.

Pediatric Nuclear Medicine Categorical Course
June 18, 1990
Washington, USA
Further details: Society of Nuclear Medicine, 136 Madison Avenue, New York, NY 10016-6760, USA.

Sixth Annual Physics and Biology of Radiology
August 23–28, 1990
San Diego; USA
Further details: Dawne Ryals, Ryals & Associates, PO Box 1925, Roswell, GA 30077-1925, USA. Tel: 404 641 9773.

16th L. H. Gray Memorial Conference Vasculature as a Target for Anti-Cancer Therapy
September 17–21, 1990
Manchester
Further details: Dr J. V. Moore, Paterson Institute of Cancer Research, Christie Hospital and Holt Radium Institute, Wilmslow Road, Manchester M20 9BX. Tel: 061-445 8123, Ext. 518.

Radiology in Britain and Belgium
September 23–30, 1990
Eastbourne and Brussels
Further details: D. Beatty Crawford, MD, Department of Radiology, University of Connecticut Health Center, Farmington, CT 06032, USA. Tel: 203 679 3322.

As a service to our readers, notice of meetings or courses will be inserted free of charge. Please send full details to the Honorary Editor, BIR Bulletin.

Please send articles for the Bulletin or any comments or suggestions you may have about the Bulletin to The Honorary Editor, BIR Bulletin, 36 Portland Place, London W1N 4AT.